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(54) Title: TRICYCLIC DIAZEPINES AS TOCOLYTIC OXYTOCIN RECEPTOR ANTAGONISTS

(57) Abstract: This invention provides novel tricyclic diazepine compounds as well as methods and pharmaceutical compositions utilizing these compounds for the treatment and/or prevention and/or suppression of disorders which may be remedied or alleviated by oxytocin antagonist acivity, including treatment of preterm labor, dysmerorrhea, endometritis, and for suppressing labor prior to caesarean delivery. These compounds are also useful in enhancing fertility rates, enhancing survival rates and synchronizing estrus in farm animals; and may be useful in the prevention and treatment of disfunctions of the oxytocin system in the central nervous system including obsessive compulsive disorder (OCD) and neuropsychiatric disorders.

TRICYCLIC DIAZEPINES AS TOCOLYTIC OXYTOCIN RECEPTOR ANTAGONISTS

This invention concerns novel tricyclic diazepines which act as competitive oxytocin receptor antagonists, as well as methods of their manufacture, methods of treatment and pharmaceutical compositions utilizing these compounds.

The compounds of the present invention are useful therapeutic agents in mammals, particularly in humans. More specifically, they can be used in the prevention and/or suppression of preterm labor, for the suppression of labor at term prior to caesarean delivery, to facilitate antinatal transport to a medical facility, and for the treatment of dysmenorrhea. These compounds also useful in enhancing fertility rates, enhancing survival rates and synchronizing estrus in farm animals; and may be useful in the prevention and treatment of disfunctions of the oxytocin system in the central nervous system including obsessive compulsive disorder (OCD) and neuropsychiatric disorders.

Background of the Invention

Premature labor remains the leading cause of perinatal mortality and morbidity. Infant mortality dramatically decreases with increased gestational age. The survival rate of prematurely born infants increases from 20% at 24 weeks to 94% at 30 weeks. Moreover the cost associated with the care of an infant born prematurely is extremely high. While many agents have been developed for the treatment of premature labor in the last 40 years, the incidence of pre-term births and low birth weight infants has remained relatively unchanged. Therefore there remains an unmet need for the development of a safe and effective treatment of preterm labor.

Tocolytic (uterine relaxing) agents currently in use include β_2 adrenergic receptor agonists such as Ritodrine which is moderately effective in suppressing preterm labor, but it is associated with maternal hypotension, tachycardia, and metabolic side effects. Several other agents have been used to suppress premature labor, including other β_2 adrenergic agonists (terbutaline, albuterol), magnesium sulfate, NSAIDs (indomethacin), and calcium channel blockers. The consensus is that none of these agents are very

effective; there is no clinical evidence showing that these compounds can prolong gestation for more than 7 days (Johnson, *Drugs*, **45**, 684-692 (1993)). Furthermore, their safety profile is not ideal. Adverse effects include respiratory depression and cardiac arrest (magnesium sulfate), hemodynamic effects (calcium channel blockers), premature closure of the *ductus arteriosus* and oligohydramnios (NSAIDs; prostaglandin synthase inhibitors). Therefore, there is an unmet need for safer and more efficacious agents for the treatment of preterm labor with better patient tolerability. Specific requirements with regard to safety include a product with no or low rates of tachycardia, limited anxiety, improved fetal safety, and few, if any, adverse cardiovascular effects.

One target of interest is the oxytocin receptor in the uterus, and a selective oxytocin receptor antagonist has been proposed as an ideal tocolytic agent. While the exact role of oxytocin (OT) in parturition has not been clearly defined, there is evidence strongly suggesting that it may play a critical role in the initiation and progression of labor in humans (Fuchs et al. *Science* **215**, 1396-1398 (1982); Maggi et al. *J. Clin. Endocrinol. Metab.* **70**, 1142-1154 (1990); Åkerlund, *Reg.. Pept.* **45**, 187-191 (1993); Åkerlund, Int. Congr. Symp. Semin. Ser., *Progress in Endocrinology* **3**, 657-660 (1993); Åkerlund et al., in *Oxytocin*, Ed. R. Ivell and J. Russel, Plenum Press, New York, pp 595-600 (1995)). Preliminary clinical trials with oxytocin receptor antagonists support the concept that a blockade of OT receptors reduces uterine myometrial activity and delays the onset of labor (Åkerlund et al., *Br. J. Obst. Gynaecol.* **94**, 1040-1044, (1987); Andersen et al., *Am. J. Perinatol.* **6**, 196-199 (1989); Melin, *Reg.. Pept.* **45**, 285-288 (1993)). Thus, a selective oxytocin antagonist is expected to block the major effects of oxytocin exerted mainly on the uterus at term, and to be more efficacious than current therapies for the treatment of preterm labor. By virtue of its direct action on the receptors in the uterus an oxytocin antagonist is also expected to have fewer side effects and an improved safety profile.

The following prior art references describe peptidic oxytocin antagonists: Hruby et al., Structure-Activity Relationships of Neurohypophyseal Peptides, in *The Peptides: Analysis, Synthesis and Biology*; Udenfriend and Meienhofer Eds., Academic Press, New York, Vol. 8, 77-207 (1987); Pettibone et al., *Endocrinology*, **125**, 217 (1989); Manning et al., Synthesis and Some Uses of Receptor-Specific Agonists and Antagonists of Vasopressin and Oxytocin, *J. Recept. Res.*, **13**, 195-214 (1993); Goodwin

et al., Dose Ranging Study of the Oxytocin Antagonist Atosiban in the Treatment of Preterm Labor, *Obstet. Gynecol.*, **88**, 331-336 (1996). Peptidic oxytocin antagonists suffer from a lack of oral activity and many of these peptides are non-selective antagonists since they also exhibit vasopressin antagonist activity. Bock et al. [*J. Med. Chem.* **33**, 2321 (1990)], Pettibone et al. [*J. Pharm. Exp. Ther.* **256**, 304 (1991)], and Williams et al. [*J. Med. Chem.*, **35**, 3905 (1992)] have reported on potent hexapeptide oxytocin antagonists which also exhibit weak vasopressin antagonistic activity in binding to V_1 and V_2 receptors.

Various non-peptidic oxytocin antagonists and/or oxytocin/vasopressin (AVP) antagonists have recently been reported by Pettibone et al., *Endocrinology*, **125**, 217 (1989); Yamamura et al., *Science*, **252**, 572-574 (1991); Evans et al., *J. Med. Chem.*, **35**, 3919-3927 (1992); Pettibone et al., *J. Pharmacol. Exp. Ther*, **264**, 308-314 (1992); Ohnishi et al., J. *Clin. Pharmacol.* **33**, 230-238, (1993); Evans et al., *J. Med. Chem.* **36**, 3993-4006 (1993); Pettibone et al., *Drug Dev. Res.* **30**, 129-142 (1993); Freidinger et al., General Strategies in Peptidomimetic Design: Applications to Oxytocin Antagonists, in *Perspect. Med. Chem.* 179-193 (1993), Ed. B. Testa, Verlag, Basel, Switzerland; Serradeil-Legal, *J. Clin. Invest.*, **92**, 224-231 (1993); Williams et al., *J. Med. Chem.* **37**, 565-571 (1994); Williams et al., *Bioorg. Med. Chem.* **2**, 971-985 (1994); Yamamura et al., *Br. J. Pharmacol.*, **105**, 546-551 (1995); Pettibone et al., *Advances in Experimental Medicine and Biology* **395**, 601-612 (1995); Williams et al., *J. Med. Chem.* **38**, 4634-4636 (1995); Hobbs et al., *Biorg. Med. Chem. Lett.* **5**, 119 (1995); Williams et al., *Curr. Pharm. Des.* **2**, 41-58 (1996); Freidinger et al., *Medicinal Research Reviews*, **17**, 1-16 (1997); Pettibone et al., *Biochem. Soc. Trans.* **25** (3), 1051-1057 (1997); Bell et al., *J. Med. Chem.* **41**, 2146-2163 (1998); Kuo et al., *Bioorg. Med. Chem. Lett.* **8**, 3081-3086 (1998); Williams et al., *Biorg. Med. Chem. Lett.* **9**, 1311-1316 (1999).

Certain carbostyril derivatives and bicyclic azepines are disclosed as oxytocin and vasopressin antagonists by Ogawa et al. in WO 94/01113 (1994); benzoxazinones are disclosed as oxytocin and vasopressin receptor antagonists by Sparks et al. in WO 97/25992 (1997); Williams et al. disclose piperidine oxytocin and vasopressin receptor antagonists in WO 96/22775 (1996); Bock et al. disclose benzoxazinone and benzopyrimidinone piperidines useful as oxytocin and vasopressin receptor antagonists in U.S. Patent 5,665,719 (1997); piperazines and spiropiperidines useful as oxytocin and

vasopressin receptor antagonists are disclosed by Evans et al. in U.S, Patent 5, 670,509 (1997) and by Bock et al. in U.S. Patent 5,756,504 (1998); Bell et al. disclose piperazine oxytocin receptor antagonists in UK Patent Application, GB 2 326 639 A (1998); Bell et al. disclose benzoxazinone and quinolinone oxytocin and vasopressin receptor antagonists in UK Patent Application GB 2 326 410 A (1998); Bell et al. disclose benzoxazinone oxytocin and vasopressin receptor antagonists in U.S. Patent 5,756,497 (1998); Matsuhisa et al. disclose difluoro tetrahydrobenzazepine derivatives as oxytocin antagonists in WO 98/39325 (1998); Ogawa et al. disclose heterocyclic bisamides with vasopressin and oxytocin antagonist activity in U.S. Patent 5,753,644 (1998)); and Ogawa et al. disclose benzazepine derivatives with anti-vasopressin activity, oxytocin antagonistic activity and vasopressin agonist activity, useful as vasopressin antagonists, vasopressin agonists and oxytocin antagonists in WO 97/22591 (1997) and U.S. Patent 6,096,736 (2000).

Trybulski et al. disclose 3-carboxamide derivatives of pyrrolobenzodiazepine bisamides with vasopressin antagonist activity in U.S. Patent 5,880,122 (1999); bicyclic thienoazepines with vasopressin and oxytocin receptor antagonist activity are disclosed by Albright et al. in WO 96/22294 (1996) and U.S. Patent 5,654,297 (1997); and tricyclic benzazepines with vasopressin and oxytocin receptor antagonist activity are disclosed by Albright et al. in U.S. Patent 5,849,735 (1998).

Albright et al. broadly disclose tricyclic benzazepine vasopressin antagonists in WO 96/22282A1 (1996) which possess antagonistic activity at the V_1 and/or V_2 receptors and exhibit in vivo vasopressin antagonistic activity, as well as antagonistic activity at the oxytocin receptors.

Venkatesan et al. broadly disclose tricyclic benzazepines with vasopressin and oxytocin antagonist activity in U.S. Patent 5,521,173 (1996), WO 96/22292 (1996), and in U.S. Patent 5,780,471 (1998) which possess antagonistic activity at the V_1 and/or V_2 receptors and exhibit in vivo vasopressin antagonistic activity, as well as antagonistic activity at the oxytocin receptors.

Compounds which behave as potent oxytocin antagonists by binding with high affinity and selectivity to the oxytocin receptors, thus preventing oxytocin from binding to

its receptors and exerting its biological and pharmacologic effects in vivo, can be useful for the treatment and/or prevention and/or suppression of preterm labor, for the suppression of term labor prior to a caesarian delivery, and to facilitate antinatal transport to a medical facility. They also can produce contraception in mammals given that oxytocin antagonists have been shown to inhibit the release of oxytocin-stimulated luteneizing hormone (LH) from pituitary cells (Rettori et al., *Proc. Nat. Acad. Sci. U.S.A.* **94**, 2741-2744 (1997); Evans et al., *J. Endocrinol.*, **122**, 107-116 (1989); Robinson et al., *J. Endocrinol.* **125**, 425-432 (1990)).

Oxytocin antagonists have the ability to relax uterine contractions induced by oxytocin in mammals and thus can be also useful for the treatment of dysmenorrhea, a condition characterized by pain during menstruation (Åkerlund, Int. Congr. Symp. Semin. Ser., *Progress in Endocrinology* **3**, 657-660 (1993); Åkerlund, *Reg. Pept.* **45**, 187-191 (1993); Melin, *Reg. Pept.* **45**, 285-288 (1993)). Primary dysmenorrhea is associated with ovulatory cycles, and it is the most common complaint of gynecologic patients. Myometrial hypercontractility and decreased blood flow to the uterus are thought to be causative factors for for the symptoms of primary dysmenorrhea (Åkerlund, *Acta Obstet. Gynecol. Scand.* **66**, 459-461 (1987). In particular, vasoconstriction of small uterine arteries by vasopressin and oxytocin is thought to produce tissue ischemia and pain (Jovanovic et al., *Br. J. Pharmacol.* **12**, 1468-1474 (91997); Chen et al., *Eur. J. Pharmacol.* **376**, 25-51 (1999)).

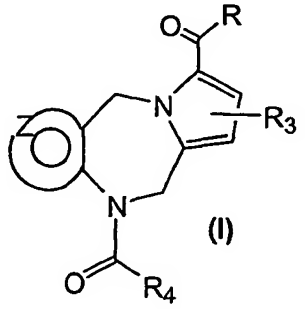
The administration of oxytocin receptor antagonists to farm animals after fertilization has been found to enhance fertility rates by blocking oxytocin induced luteolysis leading to embryonic loss (Hickey et al., WO 96/09824 A1 (1996), Sparks et al., WO 97/25992 A1 (1997); Sparks et al., U.S. Patent 5,726,172 A (1998)). Thus, oxytocin receptor antagonists can be useful in farm animal husbandry to control timing of parturition and delivery of newborns resulting in enhanced survival rates. They can also be useful for the synchronization of estrus by preventing oxytocin induced corpus luteum regression and by delaying estrus (Okano, *J. Reprod. Dev.* **42** (Suppl.), 67-70 (1996)). Furthermore oxytocin receptor antagonists have been found to have a powerful effect in inhibiting oxytocin-induced milk ejection in dairy cows (Wellnitz et al., *Journal of Dairy Research* **66**, 1-8 (1999)).

Oxytocin is also synthesized in the brain and released in the central nervous system. Recent studies have established the importance of central oxytocin in cognitive, affiliative, sexual and reproductive behavior, and in regulating feeding, grooming and response to stress in animals. Oxytocin may also influence normal behavior in humans.Modulators of oxytocin binding to its receptors in the central nervous system may be useful in the prevention and treatment of disfunctions of the oxytocin system, including obsessive compulsive disorder (OCD) and other neuropsychiatric disorders (Kovacs et al., *Psychoneuroendocrinology* **23,** 945-962 (1998); McCarthy et al., *U.K. Mol. Med. Today* **3**, 269-275 (1997); Bohus, *Peptidergic Neuron, [Int. Symp. Neurosecretion], 12th (1996),* 267-277, Publ. Birkhauser, Basel, Switz.; Leckman et al., *Psychoneuroendocrinology* **19**, 723-749 (1994)).

Competitive inhibitors of vasopressin binding to its receptors are useful in the treatment or prevention of state diseases involving vasopressin disorders in mammals, which include vasodilation and aquaresis (free-water diuresis), treating hypertension and inhibiting platelet aggregation. They are also useful in the treatment of congestive heart failure, cirrhosis with ascites, and in the syndrome of inappropriate secretion of antiduretic hormone (SIADH). Furthermore, vasopressin receptor antagonists have been found to be useful in treating disturbances or illnesses of the inner ear, particularly those related to Meniere's disease (Zenner et al., WO 99/24051-A2 (1999)); and for the prevention and treatment of ocular circulatory disorders, particularly intraocular hypertension or glaucoma and vision disorders such as shortsightedness (Ogawa et al., WO 99/38533-A1 (1999)); Ohtake et al., WO 99/65525 (1999)).

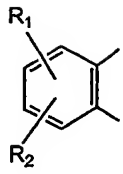
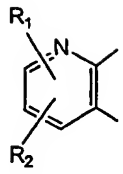
Summary of the Invention

This invention comprises compounds of Formula (I):



(I)

wherein:

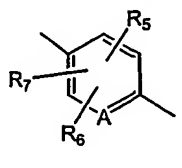
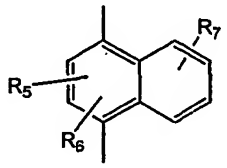
is ;

R_1 and R_2 are, independently, selected from hydrogen, $(C_1\text{-}C_6)$alkyl, halogen, cyano, trifluoromethyl, hydroxy, amino, $(C_1\text{-}C_6)$alkylamino, $(C_1\text{-}C_6)$alkoxy, $-OCF_3$, $(C_1\text{-}C_6)$alkoxy-carbonyl, -NHCO[$(C_1\text{-}C_6)$alkyl], carboxy, $-CONH_2$, –CONH[$(C_1\text{-}C_6)$alkyl], or –CON[$(C_1\text{-}C_6)$alkyl]$_2$;

R_3 is a substituent selected from hydrogen, $(C_1\text{-}C_6$)alkyl, $(C_1\text{-}C_6)$alkoxy, hydroxy, amino, $(C_1\text{-}C_6)$alkylamino, -COalkyl$(C_1\text{-}C_6)$, or halogen;

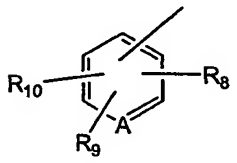
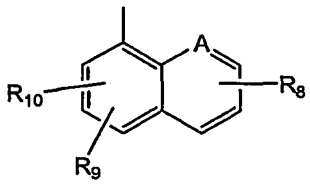
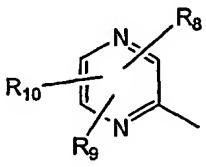
R_4 consists of the moiety **B-C**; wherein:

B is selected from the group of:

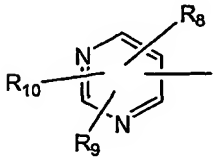
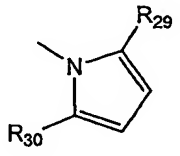



(a) (b)

and **C** is selected from the group of:

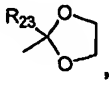
(c) (d) (e)

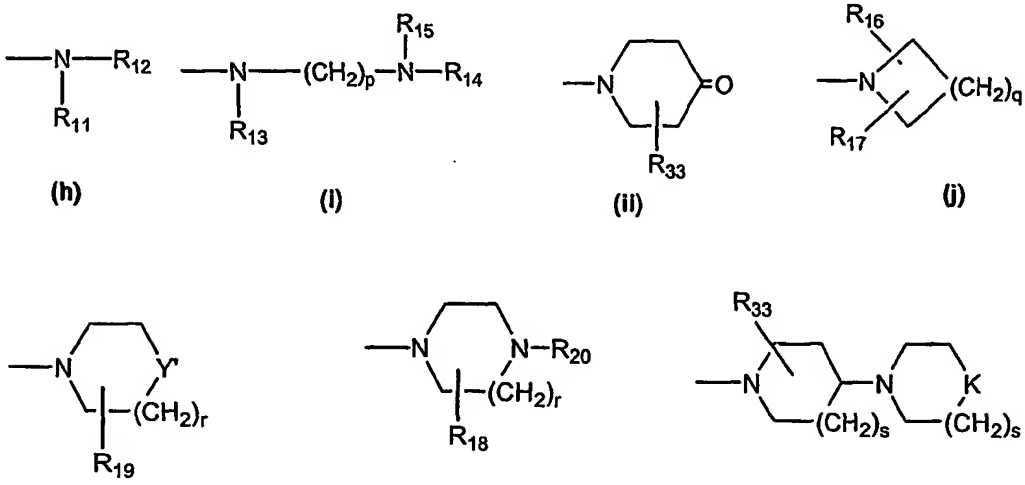
(f) (g)

wherein:

A is CH or N;

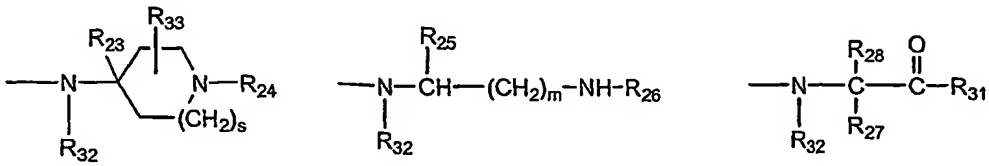
R_5, R_6 , R_7, R_8, R_9, R_{10} are, independently, selected from hydrogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkyl-carbonyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, hydroxy(C_1-C_6)alkyl, lower alkoxy-(C_1-C_6)alkyl, acyloxy-(C_1-C_6)alkyl, (C_3-C_8)cycloalkyl, formyl, (C_3-C_8)cycloalkyl-carbonyl, carboxy, lower alkoxy-carbonyl, (C_3-C_8)cycloalkyloxy-carbonyl, aryllowеralkyloxy-carbonyl, carbamoyl, -O-CH_2-CH=CH_2, halogen, halolowеralkyl including trifluoromethyl, -OCF_3, -S[(C_1-C_6)alkyl], -OC(O)N[(C_1-C_6)alkyl]$_2$, -CONH[(C_1-C_6)alkyl], -CON[(C_1-C_6)alkyl]$_2$, (C_1-C_6)alkylamino, di-[(C_1-C_6)alkyl] amino, (C_1-C_6)alkyl di-[(C_1-C_6)alkyl]amino, hydroxy, cyano, trifluoro-methylthio, nitro, amino, (C_1-C_6)alkylsulfonyl, aminosulfonyl, (C_1-C_6)alkylamino-sulfonyl,  , phenyl or naphthyl;

and R is selected from -OH, $NHOR_{36}$, or any of the following groups:

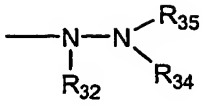


(h) (i) (ii) (j)

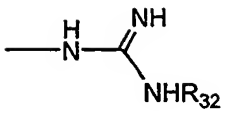
(k) (l) o



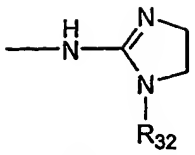
(t) (u) (v)



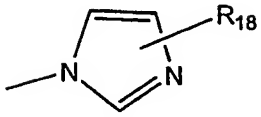
(w)



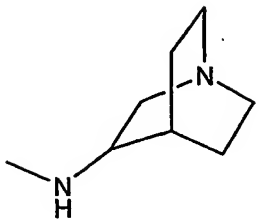
(x)



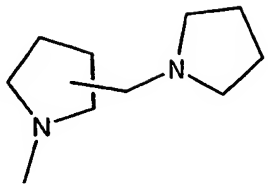
(y)



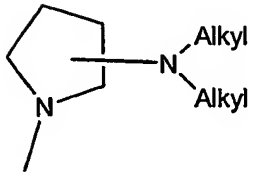
(z)



(z')



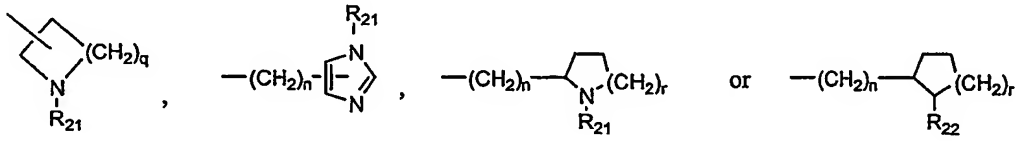
(z")



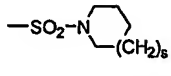
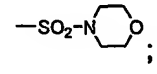
(z"')

wherein:

R_{11} and R_{12} are, independently, selected from hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_3\text{-}C_8)$cycloalkyl optionally mono- or di-[$(C_1\text{-}C_6)$alkyl] substituted, polycycloalkyl having 2 or 3 rings and from 6 to 15 ring carbon atoms and optionally a ring nitrogen atom; said polycyclic group being optionally bonded through lower alkyl including but not limited to adamantanyl, adamantine-lower alkyl, bornyl, norbornyl, or quinuclidyl;



$(C_3\text{-}C_8)$cycloalkyl-lower alkyl, halo lower alkyl, cyano lower alkyl, lower alkyl thiol, loweralkoxy-carbonyl lower alkyl, loweralkylthio lower alkyl, indolyl lower alkyl; aryl, optionally substituted with 1 to three substituents selected from the group of lower alkyl, hydroxy, $(C_1\text{-}C_6)$alkoxy, aryl lower alkoxy, halogen, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2F$, $-OCH_2CF_3$, $-OCF_2CF_3$, $-OCH_2CHF_2$, alkylamido lower alkyl,

dialkylamido lower alkyl, morpholinyl, thiomorpholinyl, pyrrolidinyl, piperidinyl, $-SCF_3$, $-SO_2$[lower alkyl], sulfonyl cycloalkyl,  or  ; or (C_7-C_{12}) arylalkyl, wherein the aryl moiety is optionally substituted with halogen or alkoxy; with the proviso that R_{11} and R_{12} can be taken together with the nitrogen to which they are attached to form a 5-8 membered unsaturated heteroaromatic ring containing 2 nitrogen atoms;

R_{13} is selected from hydrogen, (C_1-C_6)alkyl, (C_7-C_{12})aralkyl, or-$(CH_2)_p$-N(lower alkyl)$_2$;

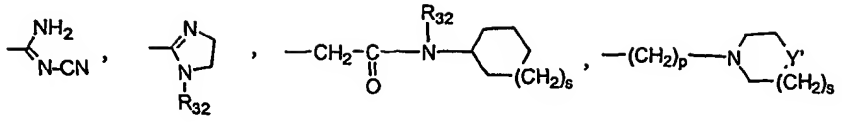
R_{14} and R_{15} are, independently, selected from hydrogen, (C_1-C_6)alkyl, or (C_7-C_{12}) arylalkyl, with the proviso that R_{14} and R_{15} can be taken together with the nitrogen atom to which they are attached to form a 5 to 7 membered saturated heterocycle, optionally containing one additional O or S atom (all of the above rings being optionally substituted with 1 or more loweralkyl groups); or a 5-membered unsaturated heterocycle containing 1 to 3 nitrogen atoms;

R_{16} and R_{17} are, independently selected from the group of hydrogen, (C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$, (C_7-C_{12}) arylalkyl, lower alkoxy-carbonyl, aryl lower alkoxy-carbonyl, $-CONH_2$, -CONH [(C_1-C_6)alkyl], -CON [(C_1-C_6)alkyl]$_2$; (C_3-C_8)cycloalkylamino (C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$amino; with the proviso that R_{16} and R_{17} can be joined to form a 5 to 6 membered saturated ring to provide a bicyclic system, optionally containing one or more alkyl groups including, but not limited to, 1,3,3-trimethyl-6-aza-bicyclo[3.2.1]octane;

R_{18} is one to three substituents selected independently from the group of hydrogen, or (C_1-C_6)alkyl;

R_{19} is selcted from the group of hydrogen, (C_1-C_6)alkyl, -N[(C_1-C_6)alkyl]$_2$, or (C_3-C_8)cycloalkylamine when Y'= CH_2; or it is selected from the group of hydrogen and (C_1-C_6)alkyl when Y' = X';

R_{20} is selected from the group of hydrogen, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_8)cycloalkyl, $-CONH_2$, -CON[lower alkyl]$_2$, carbonyl lower alkyl, lower alkyl CONH[lower alkyl], lower alkyl CON[lower alkyl]$_2$, (C_3-C_8)cycloalkylamino carbonyl, (C_3-C_8)cycloalkylamino carbonyl lower alkyl, arylamino carbonyl lower alkyl, lower alkoxy-carbonyl, lower alkoxy-carbonyl lower alkyl, -$(CH_2)_p$-N[lower alkyl]$_2$, -$(CH_2)_p$-N[lower alkenyl]$_2$, -CH[aryl]$_2$ wherein the aryl is optionally substituted by (C_1-C_6)alkyl, (C_1-C_6)alkoxy, or halogen;



benzodioxolyl, benzodioxolyl lower alkyl, benzodioxanyl, benzodioxanyl lower alkyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, furancarbonyl, -SO_2[lower alkyl], aryl optionally substituted by one to three substituents selected independently, from the group of hydrogen, halogen, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, lower alkoxy, -CF_3, -OCF_3, -OCH_2CF_3, -$OCHF_2$, -OCH_2F, -OCF_2CF_3, -OCH_2CHF_2, -CO lower alkyl, -CN, nitro, -SCH_3, aryl lower alkoxy, aryl lower alkoxy carbonyl, indolyl, morpholino or thiomorpholino; or (C_7-C_{12})aralkyl wherein the aryl moiety is optionally substituted with halogen, (C_1-C_6)alkyl, or (C_1-C_6)alkoxy;

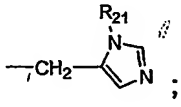
R_{21} and R_{22} are selected, independently, from the group of hydrogen, (C_1-C_6)alkyl, or (C_7-C_{12}) arylalkyl;

R_{23} is selected from hydrogen, or (C_1-C_6)alkyl ;

R_{24} is selected from the group of (C_1-C_6)alkyl, (C_7-C_{12})arylalkyl, lower alkoxycarbonyl, or SO_2[(C_1-C_6)alkyl];

R_{25} is selected from (C_1-C_6)alkyl, (C_7-C_{12})arylalkyl, lower alkoxyl-carbonyl, aryl lower alkoxy-carbonyl, -COOH, -$CONH_2$, -CONH[(C_1-C_6)alkyl], -CONH[(C_7-C_{12})aryl-alkyl], -CON[(C_1-C_6)alkyl]$_2$, or -CON[(C_7-C_{12}) arylalkyl]$_2$;

R_{26} is selected from hydrogen, lower alkoxycarbonyl, fluorenylalkoxycarbonyl, aryl lower alkyl, or aryl lower alkoxycarbonyl;

R_{27} and R_{28} are, independently, selected from the group of hydrogen, lower alkyl, aryl lower alkyl (the aryl moiety being optionally substituted by hydroxy, alkoxy, or halogen), or  ; with the proviso that R_{27} and R_{28} can be taken together with the carbon to which they are attached to form a 3 to 6-membered saturated ring;

R_{29} and R_{30} are, independently, selected from the group of hydrogen, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_8)cycloalkyl, or aryl [optionally substituted by hydroxy, (C_1-C_6) lower alkoxy, (C_1-C_6)alkyl, halo, cyano, -SO_2 [(C_1-C_6) lower alkyl, or –S[(C_1-C_6) lower alkyl];

R_{31} is selected from the group of hydroxy, $(C_1\text{-}C_6)$alkoxy, aryl lower alkoxy, amino, -NH[$(C_1\text{-}C_6)$alkyl], or –N[$(C_1\text{-}C_6)$alkyl]$_2$;

R_{32} is selected from the group of hydrogen, or $(C_1\text{-}C_6)$alkyl;

R_{33} is one to three substituents selected from the group of hydrogen, or $(C_1\text{-}C_6)$alkyl;

R_{34} and R_{35} are, independently, selected from the group of hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_7\text{-}C_{12})$ arylalkyl, with the proviso that R_{34} and R_{35} taken together with the nitrogen atom to which they are attached, may form a 4 to 8 membered saturated heterocycle, optionally containing one additional O, S or N[$(C_1\text{-}C_6)$ lower alkyl], all the above rings being optionally substituted with 1 or more alkyl groups; or a 5 membered unsaturated heterocycle containing 2 to 3 nitrogen atoms;

R_{36} is selected from the group of hydrogen, or $(C_1\text{-}C_6)$alkyl;

X' is O, S, SO, SO_2;

Y'= CH_2 or X';

K= Y' or N[$(C_1\text{-}C_6)$];

m is an integer from 1 to 4;

n is an integer from 1 to 4;

p is an integer from 2 to 4 ;

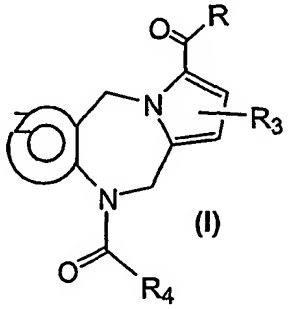
q is an integer from 1 to 5;

r is an integer from 1 to 2;

s is an integer from 0 to 1;

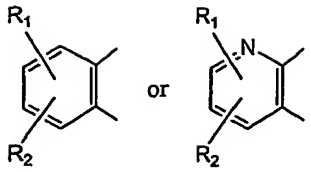
and the pharmaceutically acceptable salts, or pro-drug forms thereof.

Among the preferred compounds of this invention are those of the formula:



(I)

wherein:


is 

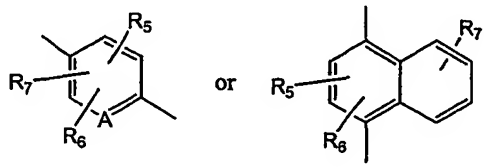
;

R_1 and R_2 are, independently, selected from hydrogen, (C_1-C_6)alkyl, halogen, cyano, trifluoromethyl, hydroxy, amino, (C_1-C_6)alkylamino, (C_1-C_6)alkoxy, -OCF_3, (C_1-C_6)alkoxy carbonyl, -NHCO[(C_1-C_6)alkyl], carboxy, -$CONH_2$, –CONH[(C_1-C_6)alkyl], or –CON[(C_1-C_6)alkyl]$_2$;

R_3 is a substituent selected from hydrogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, hydroxy, amino, (C_1-C_6)alkylamino, -COalkyl(C_1-C_6), or halogen;

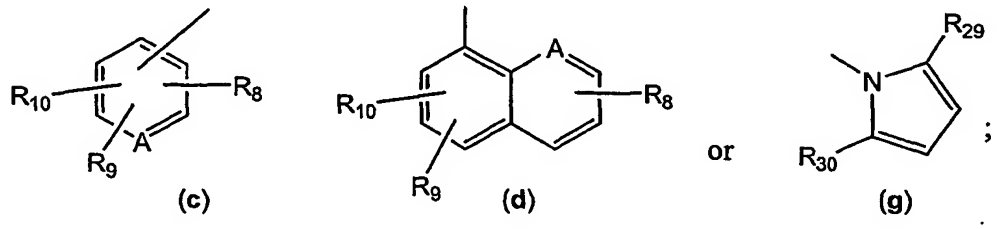
R_4 consists of the moiety **B-C**; wherein:

B is selected from the group of:



(a) (b)

and **C** is selected from the group of:



(c) (d) (g)
;

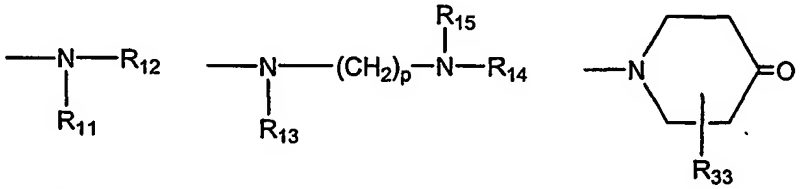
wherein:

A is CH or N;

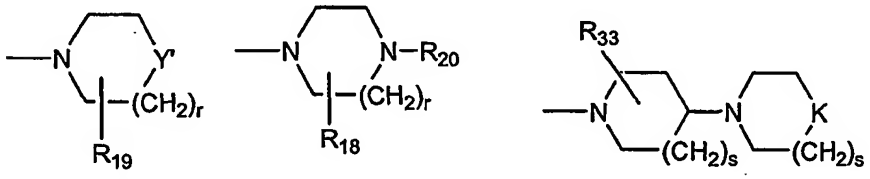
R_5, R_6 , R_7, R_8, R_9, R_{10} are independently selected from hydrogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkyl-carbonyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, hydroxy(C_1-C_6)alkyl, loweralkoxy-(C_1-C_6)alkyl, acyloxy-(C_1-C_6)alkyl, (C_3-C_8)cycloalkyl, formyl, (C_3-C_8)cycloalkyl-carbonyl, carboxy, lower alkoxy-carbonyl, (C_3-C_8)cycloalkyloxy-carbonyl, carbamoyl, -O-CH_2-CH=CH_2, halogen, halo lower alkyl including trifluoromethyl, -OCF_3, -S[(C_1-C_6)alkyl], -OC(O)N[(C_1-C_6)alkyl]$_2$, -CONH[(C_1-C_6)alkyl], -CON[(C_1-C_6)alkyl]$_2$, (C_1-C_6)alkylamino, di-[(C_1-C_6)alkyl] amino, (C_1-C_6)alkyl di-[(C_1-C_6)alkyl]amino, hydroxy, cyano, trifluoromethylthio, nitro, amino, (C_1-C_6)alkylsulfonyl, aminosulfonyl, or (C_1-C_6)alkylaminosulfonyl;

R_{29} and R_{30} are, independently, selected from the group of H, C_1-C_6alkyl, (C_2-C_6)alkenyl, C_2-C_6alkynyl, or cycloC_3-C_6alkyl;

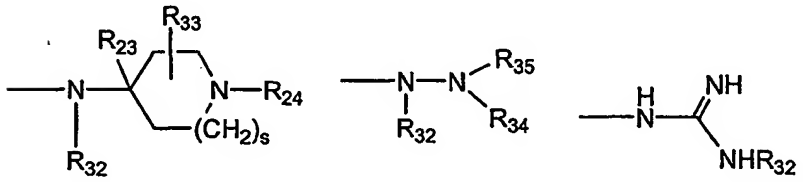
R is selected from lower alkyl, $-NHNH_2$, $-NHOR_{31}$; or $-CH=CH-N[R_{32}]_2$; lower alkoxy; phenyl optionally substituted by from one to three substituents selected from (C_1-C_6)alkyl or halogen ; or a moiety of the formulae:



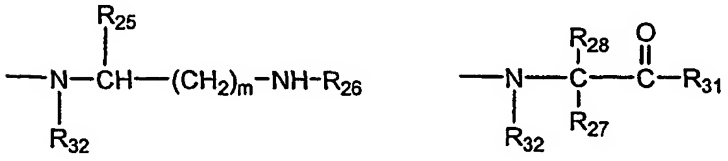
(h) (i) (ii)



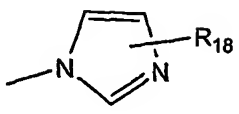
(k) (l) (o)



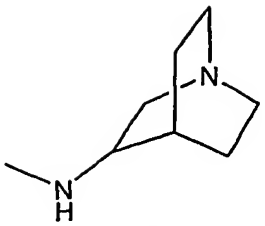
(t) (w) (x)



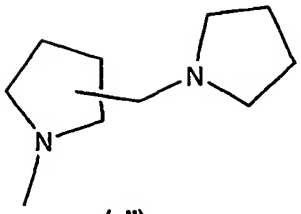
(u) (v)



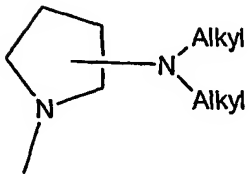
(z)



(z')

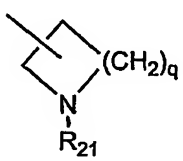


(z")

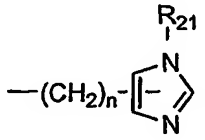


(z"')

R_{11} and R_{12} are, independently, selected from hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_3\text{-}C_8)$cycloalkyl optionally mono- or di-[$(C_1\text{-}C_6)$alkyl] substituted, $(C_3\text{-}C_8)$cycloalkyl-lower alkyl, halo lower alkyl, cyano lower alkyl, lower alkyl thiol, loweralkoxycarbonyl lower alkyl, or loweralkylthio lower alkyl; or a moiety of the formulae:

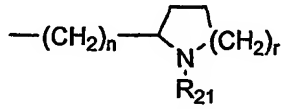


,



,

or



;

R_{13} is selected from hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_7\text{-}C_{12})$aralkyl, or-$(CH_2)_p$-N(lower alkyl)$_2$;

R_{14} and R_{15} are, independently, selected from hydrogen, $(C_1\text{-}C_6)$alkyl, with the proviso that R_{14} and R_{15} can be taken together with the nitrogen atom to which they are attached to form:

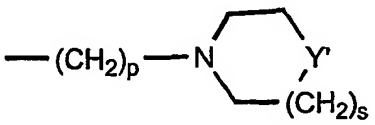
a) a 5 to 7 membered saturated heterocycle, optionally substituted with 1 or more alkyl groups; or

b) a 5-membered unsaturated heterocycle containing 1 to 3 nitrogen atoms;

R_{18} is one to three substituents selected independently from the group of hydrogen, or $(C_1\text{-}C_6)$alkyl;

R_{19} is selcted from the group of hydrogen, $(C_1\text{-}C_6)$alkyl, $-N[(C_1\text{-}C_6)alkyl]_2$, or $(C_3\text{-}C_8)$cycloalkylamine when Y'= CH_2; or it is selected from the group of hydrogen and $(C_1\text{-}C_6)$alkyl when Y' = X';

R_{20} is selected from the group of hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_3\text{-}C_8)$cycloalkyl, $-CONH_2$, -CON[lower alkyl]$_2$, carbonyl lower alkyl, lower alkyl CONH[lower alkyl], lower alkyl CON[lower alkyl]$_2$, lower alkoxy carbonyl, $(CH_2)_p$-N[lower alkyl]$_2$, $-(CH_2)_p$-N[lower alkenyl]$_2$, -CH[phenyl]$_2$ wherein the phenyl ring is optionally substituted by $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, or halogen; or R_{20} is a moiety of the formula:



;

R_{21} and R_{22} are selected, independently, from the group of hydrogen, $(C_1\text{-}C_6)$alkyl, or $(C_7\text{-}C_{12})$ arylalkyl;

R_{23} is selected from hydrogen, cyano or $(C_1\text{-}C_6)$alkyl ;

R_{24} is selected from the group of $(C_1\text{-}C_6)$alkyl, lower alkoxycarbonyl, or $SO_2[(C_1\text{-}C_6)alkyl]$;

R_{25} is selected from $(C_1\text{-}C_6)$alkyl, lower alkoxycarbonyl, $-COOH$, $-CONH_2$, $-CONH[(C_1\text{-}C_6)alkyl)]$, or $-CON[(C_1\text{-}C_6)alkyl)]_2$;

R_{26} is selected from hydrogen, lower alkoxycarbonyl, or fluorenylalkoxycarbonyl;

R_{27} and R_{28} are, independently, selected from the group of hydrogen or lower alkyl; with the proviso that R_{27} and R_{28} can be taken together with the carbon to which they are attached to form a 3 to 6-membered saturated ring;

R_{31} is selected from the group of hydroxy, $(C_1\text{-}C_6)$alkoxy, amino, $-NH[(C_1\text{-}C_6)alkyl]$, or $-N[(C_1\text{-}C_6)alkyl]_2$;

R_{32} is elected from the group of hydrogen, or $(C_1\text{-}C_6)$alkyl;

R_{33} is one to three substituents selected from the group of hydrogen, or $(C_1\text{-}C_6)$alkyl;

R_{34} and R_{35} are, independently, selected from the group of hydrogen, or $(C_1\text{-}C_6)$alkyl, with the proviso that R_{34} and R_{35} taken together with the nitrogen atom to which they are attached, may form a 5 membered unsaturated heterocycle containing 2 to 3 nitrogen atoms;

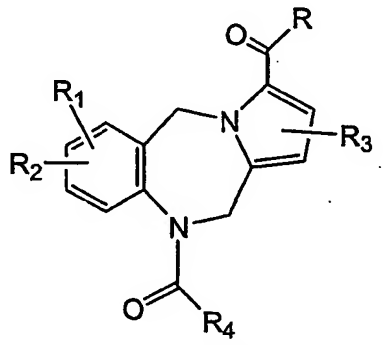
X' is O;

Y'= CH_2 or X';

K= Y' or $N[(C_1\text{-}C_6)alkyl]$;

m is an integer from 1 to 4;
n is an integer from 1 to 4;
p is an integer from 2 to 4 ;
q is an integer from 1 to 5 ;
r is an integer from 1 to 2;
s is an integer from 0 to 1;
and the pharmaceutically acceptable salts, or pro-drug forms thereof.

Within each of the groups of compounds described herein is a further subset of compounds having the general formula:



wherein R, R_1, R_2, R_3 and R_4 are as defined in the relevant group, or a pharmaceutically acceptable salt form thereof. A further subset of each of these groups includes those compounds wherein R_1, R_2 and R_3 are each hydrogen and all other variables are as described in the relevant group, or a pharmaceutically acceptable salt thereof.

Examples of alkyl as a group or part of a group, eg alkoxy or aralkyl, are carbon chains of 1 to 6 carbon atoms

As used herein the term "lower" in relation to carbon chains, such as alkoxy, alkyl, alkynyl, alkenyl, etc., is understood to refer to those groups having up to 6 carbon atoms eg 1-6, 2-6. Halogen refers to fluorine, chlorine, bromine or iodine. Cycloalkyl, whether used separately or as a part of a combined moiety, refers to cycloalkyl groups from 3 to 8 carbon atoms, preferably from 3 to 6 carbon atoms.

The term aryl as a group or part of a group, eg arylalkyl, includes carbocyclic aromatic groups of 6 to 10 carbon atoms, eg phenyl or naphthyl. The term acyl includes groups of 2-7 carbon atoms such as (C_1-C_6alkyl)carbonyl.

It is understood by those practicing the art that some of the compounds of this invention depending on the definition of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{29}, and R_{30} may contain one or more asymmetric centers and may thus give rise to enantiomers and diastereomers. The present invention includes all stereoisomers including individual diastereomers and resolved, enantiomerically pure R and S stereoisomers; as well as racemates, and all other mixtures of the R and S stereoisomers and pharmaceutically acceptable salts thereof, which possess the indicated activity. Optical isomers may be obtained in pure form by standard procedures known to those skilled in the art. It is also understood that this invention encompasses all possible regioisomers, E/Z isomers, endo-exo isomers, and mixtures thereof which possess the indicated activity. Such isomers may be obtained in pure form by standard separation procedures known to those skilled in the art. It is understood also by those practicing the art that some of the compounds of this invention depending on the definition of R_5, R_6, R_8, R_9, R_{10}, R_{29} and R_{30} may be chiral due to hindered rotation, and give rise to atropisomers which can be resolved and obtained in pure form by standard procedures known to those skilled in the art. Also included in the present invention are all polymorphs and hydrates of the compounds of the present invention.

Detailed Description of the Invention

The present invention comprises the compounds described above, as well as pharmaceutical compositions containing the compounds of this invention in combination or association with one or more pharmaceutically acceptable carriers or excipients. In particular, the present invention provides a pharmaceutical composition which comprises a therapeutically or pharmaceutically effective amount of one or more compounds of this invention and a pharmaceutically acceptable carrier or excipient.

This invention also comprises methods for treating conditions in a mammal, preferably a human, which are remedied or alleviated by oxytocin antagonist activity including, but not limited to, treatment or prevention of preterm labor, dysmenorrhea and

suppressing labor prior to caesarian delivery whenever desirable in a mammal, preferably in a human. The methods comprise administering to a mammal in need thereof a pharmaceutically or therapeutically effective amount of one or more of the compounds of this invention.

The present invention also comprises combinations of the compounds of the present invention with one or more agents useful in the treatment of disorders such as preterm labor, dysmenorrhea, and stopping labor prior to caesarian delivery. More specifically, the compounds of the present invention may be effectively administered in combination with effective amounts of other tocolytic agents used in the treatment or prevention of preterm labor, dysmenorrhea or suppressing labor prior to caesarean delivery including β-adrenergic agonists, calcium channel blockers, prostaglandin synthesis inhibitors, other oxytocin antagonists (e.g. atosiban), magnesium sulfate, ethanol, and other agents useful in the treatment of said disorders. The present invention is to be understood as embracing all simultaneous or alternating treatments of any combination of the compounds of the present invention with other tocolytic agents with any pharmaceutical composition useful for the treatment of preterm labor, dysmenorrhea, and suppressing labor prior to caesarean delivery in mammals.

The compositions are preferably adapted for intravenous (both bolus and infusion) and oral administration. However, they may be adapted for other modes of administration including subcutaneous, intraperitoneal, or intramuscular administration to a human or a farm animal in need of a tocolytic agent.

The compounds of the present invention can be used in the form of salts derived from non toxic pharmaceutically acceptable acids or bases. These salts include, but are not limited to, the following: salts with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and, as the case may be, such organic acids as acetic acid, oxalic acid, citric acid, tartaric acid, succinic acid, maleic acic, benzoic acid, benzene sulfonic acid, fumaric acid, malic acid, methane sulfonic acid, pamoic acid, and para-toluen sulfonic acid . Other salts include salts with alkali metals or alkaline earth metals, such as sodium, potassium, calcium or magnesium, or with organic bases including quaternary ammonium salts. The

compounds can also be used in the form of esters, carbamates and other conventional prodrug forms, which in general, will be functional derivatives of the compounds of this invention which are readily converted to the active moiety in vivo. This is meant to include the treatment of the various conditions described hereinbefore with a compound of this invention or with a compound which is not specifically disclosed but which converts to a compound of this invention in vivo upon administration. Also included are metabolites of the compounds of the present invention defined as active species produced upon introduction of these compounds into a biological system.

When the compounds of this invention are employed for the above utilities, they may be combined with one or more pharmaceutically acceptable excipients or carriers, for example, solvents, diluents and the like, and may be administered orally in such forms as tablets, capsules (including time release and sustained release formulations), pills, dispersible powders, granules, or suspensions containing, for example, from 0.05 to 5% of suspending agent, syrups containing, for example, from about 10 to 50% of sugar, and elixirs and the like, or parenterally in the form of sterile injectable solutions, suspensions or emulsions containing from about 0.05 to 5% suspending agent in an isotonic medium. Such pharmaceutical preparations may contain, for example, from about 25 to about 90% of the active ingredient in combination with the carrier, more usually between about 5% and 60% by weight.

The effective dosage of active ingredients employed may vary depending on the particular compound or salt employed, the mode of administration, age, weight, sex and medical condition of the patient, and the severity of the condition being treated. An ordinarily skilled physician, veterinarian or clinician can readily determine and prescribe the effective amount of the agent required to prevent, counter or arrest the progress of the condition. However, in general, satisfactory results are obtained when the compounds of the invention are administered at a daily dose of from about 0.5 to about 500 mg/Kg of mammal body weight, preferably given in divided doses two to four times a day, or in a sustained release form. For most large mammals the total daily dosage is from about 0.5 to 100 mg, preferably from 0.5 to 80 mg/Kg. Dosage forms suitable for internal use comprise from about 0.05 to 500 mg of the active compound in intimate admixture with a solid or liquid pharmaceutically acceptable carrier. This dosage

re.g.imen may be adjusted to provide the optimal therapeutic response. For example, several divided doses may be administered daily or the dose may be proportionally reduced as indicated by the exigencies of the therapeutic situation.

These active compounds may be administered orally as well as by intravenous, intramuscular, or subcutaneous routes. Solid carriers include starch, lactose, dicalcium phosphate, microcrystalline cellulose, sucrose and kaolin, while liquid carriers include sterile water, polyethylene glycols, glycerol, non-ionic surfactants and edible oils such as corn, peanut and sesame oils, as are appropriate to the nature of the active ingredient and the particular form of administration desired. Adjuvants customarily employed in the preparation of pharmaceutical compositions may be advantageously included, such as flavoring agents, coloring agents, preserving agents, and antioxidants, for example vitamin E, ascorbic acid, BHT and BHA.

These active compounds may also be administered parenterally or intraperitoneally. Solutions or suspensions of these active compounds as a free base or pharmacologically acceptable salt can be prepared in water suitably mixed with a surfactant such as hydroxypropylcellulose. Dispersions can also be prepared in glycerol, liquid polyethylene glycols and mixtures thereof in oils. Under ordinary conditions of storage and use, these preparations contain a preservative to prevent the growth of microorganisms.

The pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. In all cases, the form must be sterile and must be fluid to the extent that easy injectability exists. It must be stable under conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol (e.g. glycerol, propylene glycol, and liquid polyethylene glycol), suitable mixtures thereof, and vegetable oil.

Furthermore, active compounds of the present invention can be administered intranasally using vehicles suitable for intranasal delivery, or transdermally using transdermal skin patches known to those ordinarily skilled in the art. When using a transdermal delivery system, the dosage administration will be continuous rather than in

a single or divided daily doses. The compounds of the present invention can also be administered in the form of liposome delivery system wherein the liposomal lipid bilayers are formed from a variety of phospholipids.

Compounds of the present invention may also be delivered by the use of carriers such as monoclonal antibodies to which the active compounds are coupled. The compounds of the present invention may also be coupled to soluble polymers as drug carriers or to biode.g.radable polymers useful in achieving controlled release of the active agent.

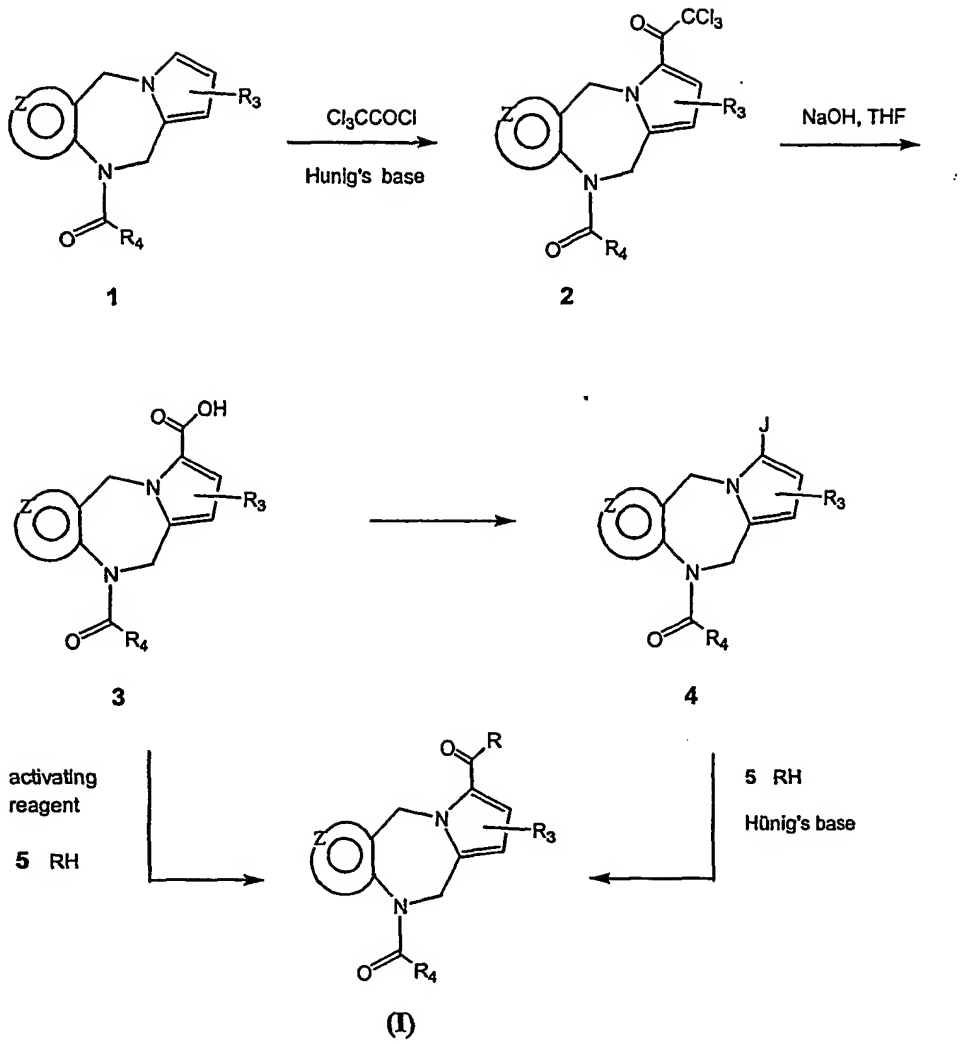
Also according to the present invention there are provided processes for producing the compounds of the present invention.

Process of the Invention

The compounds of the present invention may be prepared according to one of the general processes outlined below.

The compounds of general formula (I) wherein R_4 consists of the moiety **B-C**, where **B** is selected from the group (**a**) or (**b**) and **C** is selected from the group of (**c**), (**d**), (**e**) and (**f**) defined hereinbefore, can be conveniently prepared as shown in Scheme I.

Scheme I



According to the above preferred process, a tricyclic diazepine of formula (**1**) wherein  , R_3 and R_4 are defined hereinbefore, is reacted with perhaloalkanoyl halide preferably trichloroacetyl chloride in the presence of an organic base such as N,N-diisopropylethyl amine (Hünig's base) in an aprotic organic solvent such as dichloromethane at temperatures ranging from -10°C to ambient to provide the desired trichloroacetyl intermediate of formula (**2**). Subsequent hydrolysis of (**2**) with aqueous base such as sodium hydroxide in an organic solvent such as tetrahydrofuran or acetone

at temperatures ranging from -10°C to ambient, yields the intermediate acid of formula (**3**). The required activation of the carboxylic acid (**3**) for the subsequent coupling with a primary or secondary amine, hydroxylamine or hydrazine of formula (**5**) can be accomplished in several ways. Thus, (**3**) can be converted to an acid halide preferably a chloride or bromide of formula (**4**, J=COCl or COBr) by reaction with thionyl chloride(bromide) or oxalyl chloride(bromide) or similar reagents known in the art, either neat or in the presence of an inorganic base such as potassium carbonate, or in the presence of an organic base such as pyridine, 4-(dimethylamino)pyridine, or a tertiary amine such as triethylamine in an aprotic solvent such as dichloromethane, N,N-dimethylformamide or tetrahydrofuran at temperatures ranging from -5°C to 50°C to yield the intermediate acylated derivative (**4**). Subsequent coupling of the acid chloride(bromide) (**4**, J= COCl or COBr) with an appropriately substituted primary or secondary amine, hydroxylamine or hydrazine of formula (**5**) in the presence of a stoichiometric amount of Hünig's base in an aprotic solvent such as dichloromethane, N,N-dimethylformamide or tetrahydrofuran at temperatures ranging from ambient to the reflux temperature of the solvent provides the desired compounds of formula (**I**) wherein  , R, R_3 and R_4 are as defined hereinbefore.

Alternatively, the acylating species can be a mixed anhydride of the corresponding carboxylic acid, such as that prepared by treating said acid of formula (**3**) with 2,4,6-trichlorobenzoyl chloride in an aprotic organic solvent such as dichloromethane according to the procedure of Inanaga et al., *Bull. Chem. Soc. Jpn.* **52**, 1989 (1979). Treatment of said mixed anhydride of formula (**4**) with an appropriately substituted primary or secondary amine, hydroxylamine or hydrazine of formula (**5**) in an aprotic solvent such as dichloromethane, at temperatures ranging from ambient to the reflux temperature of the solvent provides the desired compounds of formula (**I**) wherein  , R, R_3 and R_4 are as defined hereinbefore.

Alternatively, amidation of the carboxylic acids of formula (**3**) can be effectively carried out by treatment of said acid with triphosgene in an aprotic solvent such as dichloromethane followed by reaction of the activated intermediate with an

appropriately substituted primary or secondary amine, hydroxylamine or hydrazine of formula (**5**) in the presence of an organic base such as Hünig's base at temperatures ranging from -10°C to ambient.

Another preferred process for the preparation of the compounds of the present invention of formula (**I**) wherein  , R, R_3 and R_4 are as defined hereinbefore, consists of treating the acid of formula (**3**) with an activating reagent such as N,N-dicyclohexylcarbodiimide or 1-ethyl-3-(3-dimethylamino-propyl) carbodiimide hydrochloride in the presence of 1-hydroxybenzotriazole followed by reaction of the activated intermediate with an appropriately substituted primary or secondary amine, hydroxylamine or hydrazine of formula (**5**), preferably in the presence of an organic base such as Hünig's base and a catalytic amount of 4-(dimethylamino)pyridine, in an aprotic solvent such as dichloromethane, N,N-dimethylformamide or tetrahydrofuran, at temperatures ranging from -10°C to ambient.

In another preferred process, said acid (**3**) can be activated by treatment with other activating agents such as N,N'carbonyldiimidazole, in an aprotic solvent such as dichloromethane or tetrahydrofuran, at temperatures ranging from -10°C to the reflux temperature of the solvent. Subsequent reaction of the intermediate activated imidazolide with an appropriately substituted primary or secondary amine, hydroxylamine or hydrazine of formula (**5**) provides the desired compounds of formula (**I**) wherein  , R, R_3 and R_4 are as defined hereinbefore.

Alternatively, the coupling of the appropriately substituted primary or secondary amine of formula (**5**) with said acid of formula (**3**) can be effectively carried out by using hydroxybenzotriazole tetramethyluronium hexafluorophosphate as the coupling reagent in the presence of an organic base such as Hünig's base, and in a solvent such as N,N-dimethylformamide, at temperatures ranging from -10°C to ambient to provide in good isolated yield and purity the desired compounds of formula (**I**) wherein  , R, R_3 and R_4 are as defined hereinbefore.

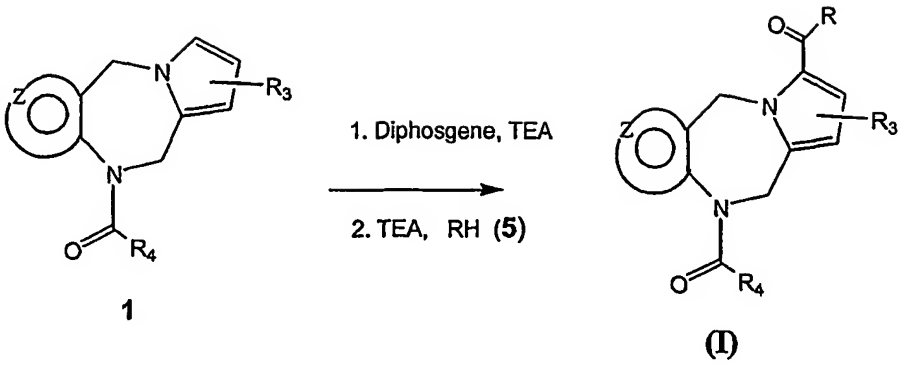
Related coupling reagents such as diphenylphosphoryl azide, diethyl cyano phosphonate, benzotriazol-1-yl-oxy-tris-(dimethylamino) phosphonium hexafluoro-phosphate and all other reagents known in the literature that have been used in the formation of amide bonds in peptide synthesis can also be used for the preparation of compounds of formula (I) wherein  , R, R_3 and R_4 are as defined hereinbefore.

As an alternative, reaction of the intermediate 3-trihalomethylketone of formula (2) directly with an appropriately substituted primary or secondary amine, hydroxylamine or hydrazine of formula (5) also provides the desired compounds of formula (I) wherein  , R, R_3 and R_4 are as defined hereinbefore.

The method of choice for the preparation of compounds of formula (I) from the intermediate carboxylic acid (3) is ultimately chosen on the basis of its compatibility with the R, R_3 and R_4 groups, and its reactivity with the tricyclic diazepine of formula (1).

Another preferred process for the preparation of (I) of Scheme I is shown in Scheme II. A tricyclic diazepine of formula (1) is reacted with diphosgene in an aprotic solvent such as dichloromethane preferably in the presence of an organic base such as triethylamine, followed by reaction of the resulting acylated intermediate with an appropriately substituted primary or secondary amine, hydroxylamine or hydrazine of formula (5) to provide the desired compounds of formula (I) wherein  , R, R_3 and R_4 are as defined hereinbefore.

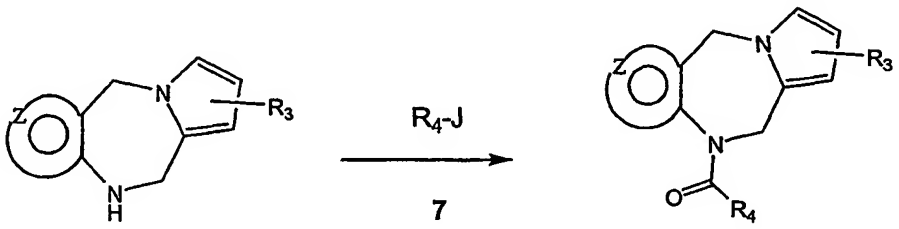
Scheme II



1 (I)

The tricyclic diazepines of formula (**1**) of Scheme (I) wherein R_4 is defined hereinbefore, can be conveniently prepared as shown in Scheme III.

Scheme III



6 1

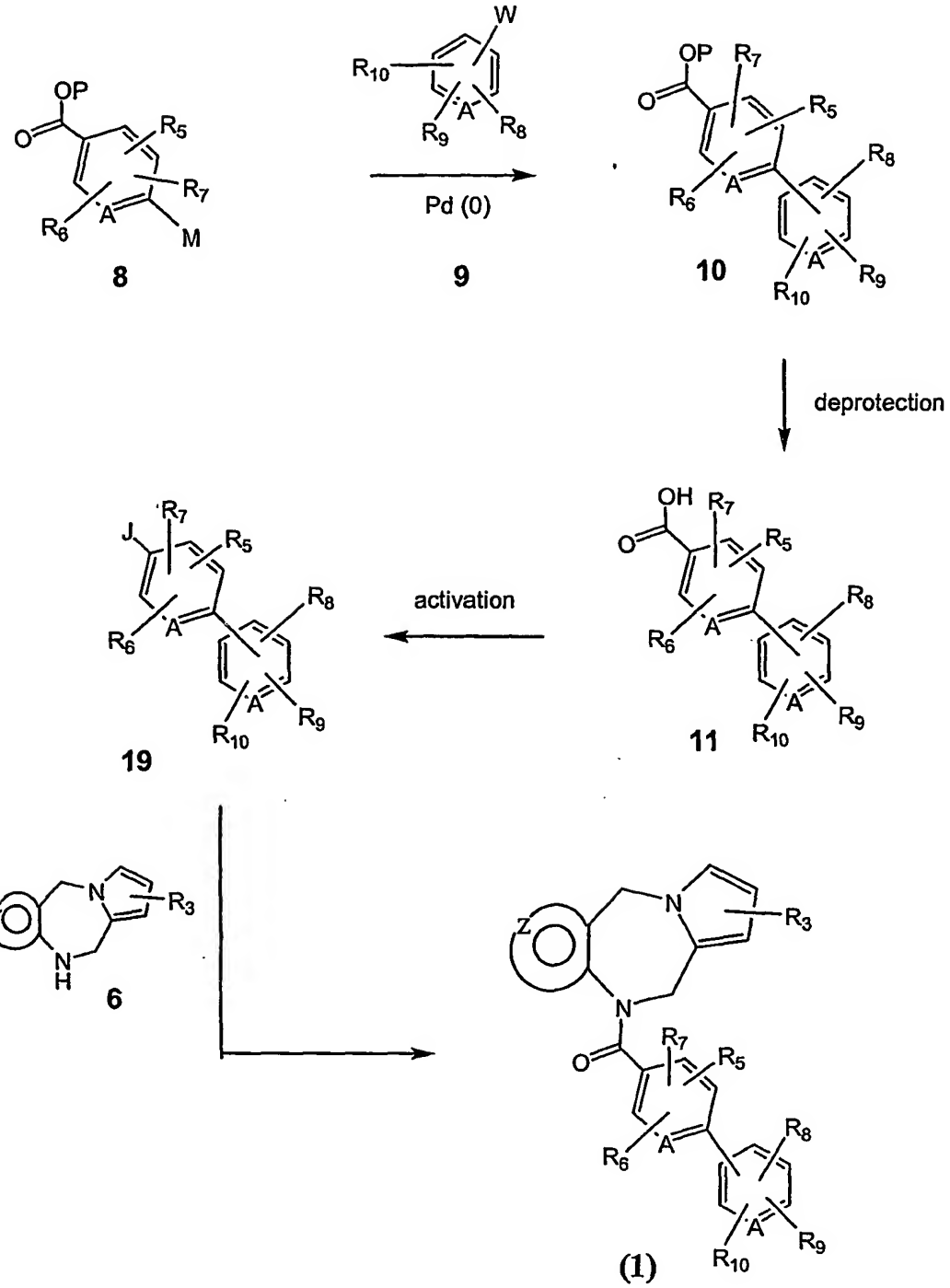
Thus, a tricyclic diazepine of formula (**6**) is treated with an appropriately substituted acylating agent such as an aroyl halide, preferably an appropriately substituted acyl chloride (or bromide) of formula (**7**, J= COCl or COBr) wherein R_4 is ultimately chosen on the basis of its compatibility with the present reaction scheme, in the presence of an inorganic base such as potassium carbonate, or in the presence of an organic base such as pyridine, 4-(dimethylamino)pyridine, or a tertiary amine such as triethylamine or N,N-diisopropylethyl amine, in an aprotic solvent such as dichloromethane, N,N-dimethylformamide or tetrahydrofuran, at temperatures ranging from -5°C to 50°C to provide intermediates of general formula (**1**) wherein R_4 is defined hereinbefore.

Alternatively, the acylating species of formula (**7**) can be a mixed anhydride of the corresponding carboxylic acid, such as that prepared by treating said acid with 2,4,6-trichlorobenzoyl chloride in an aprotic organic solvent such as dichloromethane according to the procedure of Inanaga et al., *Bull. Chem. Soc. Jpn.*, **52**, 1989 (1979). Treatment of said mixed anhydride of general formula (**7**) with a tricyclic diazepine of formula (**6**) in a solvent such as dichloromethane and in the presence of an organic base such as 4-(dimethylamino)pyridine at temperatures ranging from 0°C to the reflux temperature of the solvent, yields the intermediate acylated derivative (**1**) of Scheme **III**.

The acylating intermediate of formula (**7**) is ultimately chosen on the basis of its compatibility with the R_4 groups, and its reactivity with the tricyclic diazepine of formula (**6**).

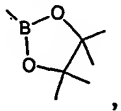
The desired intermediates of formula (**7**) of Scheme **III** wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**) and **C** is (**c**) can be conveniently prepared by a process shown in Scheme **IV**. Thus, an appropriately substituted aryl(heteroaryl) iodide (bromide, chloride, or trifluoromethane sulfonate) of formula (**8**, wherein *P* is a carboxylic acid protecting group, preferably *P*= alkyl or benzyl, M= I, Br, Cl, OTf), and A, R_5, R_6 and R_7 are defined hereinbefore, is reacted with an aryl(heteroaryl) tri(alkyl)tin(IV) derivative of formula (**9**, W= Sn(trialkyl)$_3$, preferably Sn(*n*-Bu)$_3$) wherein A, R_8, R_9 and R_{10} are defined hereinbefore, in the presence of a Pd(0) catalyst in the presence or absence of inorganic salts (e.g. LiCl), to provide the intermediate ester (**10**). Subsequent unmasking of the carboxylic acid by hydrolysis, hydrogenolysis or similar methods known in the art, followed by activation of the intermediate acid (**11**) provides the desired intermediates of formula (**19**) wherein A, R_5, R_6, R_7, R_8, R_9 and R_{10} are hereinbefore defined, suitable for coupling with the tricyclic diazepine of formula (**6**).

Scheme IV


OP
O
R5
R7
R6
A
M
8
W
R10
R9
A
R8
Pd (0)
9
OP
R7
O
R5
R8
R6
A
A
R9
R10
10
deprotection
OH
R7
O
R5
R8
R6
A
A
R9
R10
11
activation
J
R7
R5
R8
R6
A
A
R9
R10
19
N
R3
Z
N
H
6
N
R3
Z
N
O
R7
R5
R8
R6
A
A
R9
R10
(1)

The desired intermediates of formula (**7**) of Scheme **III** wherein R_4 consists of the moiety **B-C** where **B** is (**a**) and **C** is (**d**), (**e**) or (**f**) or **B** is (**b**) and **C** is either (**c**), (**d**), (**e**) or (**f**) can be prepared by a process analogous to that exemplified in Scheme **IV** by replacing intermediates of formula (**8** and **9**) with appropriately substituted naphthyl, quinolyl, pyrimidinyl or pyrazinyl intermediates.

Alternatively, the desired intermediates of formula (**10**) of Scheme **IV** wherein R_4 consists of the moiety **B-C** where **B** is (**a**) and **C** is (**c**) can be prepared by coupling of the iodide(bromide, chloride, trifluoromethanesulfonate) (**8**, M= I, Br, Cl, or OTf) with an appropriately substituted aryl(heteroaryl) boron derivative of formula (**9**, preferably $W=B(OH)_2$) in the presence of a palladium catalyst such as palladium(II) acetate or tetrakis(triphenylphosphine) palladium(0) and an organic base such as triethylamine or an inorganic base such as sodium(potassium or cesium) carbonate with or without added tetrabutylammonium bromide(iodide), in a mixture of solvents such as toluene-ethanol-water, acetone-water, water or water-acetonitrile at temperatures ranging from ambient to the reflux temperature of the solvent (Suzuki, *Pure & Appl. Chem.* **66**, 213-222 (1994), Badone et al., *J. Org. Chem.* **62**, 7170-7173 (1997); Wolfe et al. *J. Am. Chem. Soc.* **121**, 9559 (1999); Shen, *Tetr. Letters* **38**, 5575 (1997)). The exact conditions for the Suzuki coupling of the halide and the boronic acid intermediates are chosen on the basis of the nature of the substrate and the substituents. Alternatively, the coupling of (**8**, M= I or Br) with (**9**, A= N) can be carried out by using a dialkylborane, preferably a diethylpyridoborane in the presence of an inorganic base such as potassium hydroxide and tetrabutylammonium bromide(iodide) in an aprotic solvent such as tetrahydrofuran, according to the method of Ishikura et al., *Synthesis* 936-938 (1984). The desired intermediates of formula (**10**) of Scheme **IV** can be similarly prepared from the bromide (**8**, M= Br) and the boronic acid (**9**) in a solvent such as dioxane, in the presence of potassium phosphate and a Pd(0) catalyst.

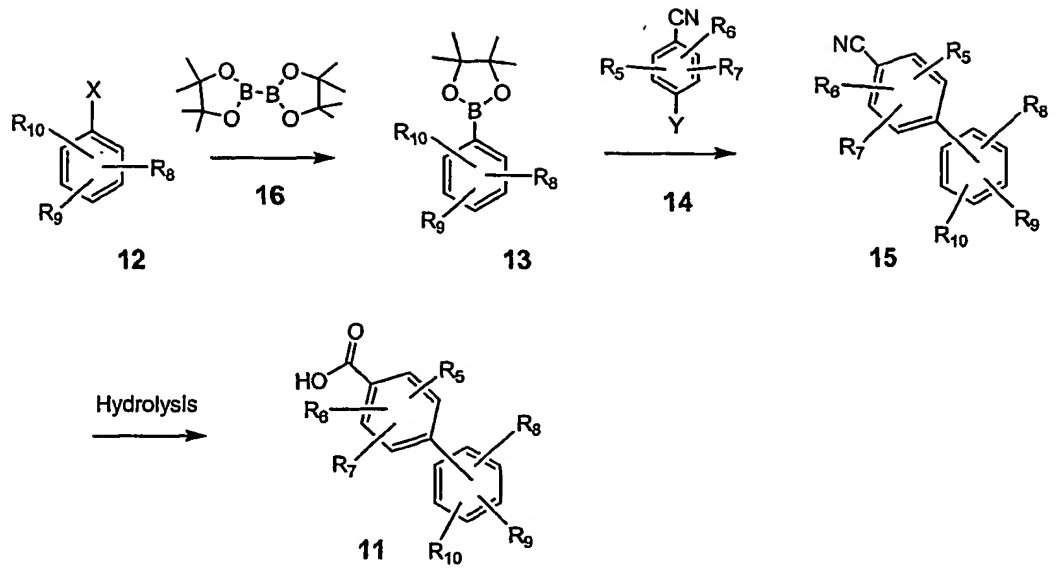
Alternatively, a cross coupling reaction of an iodide (bromide, or trifluoromethane-sulfonate) of formula (**9**, W= Br, I, OTf) with a bis(pinacolato)diboron [boronic acid, or trialkyl tin(IV)] derivative of formula (**8**, M=  , $B(OH)_2$, or $SnBu_3$) yields the desired intermediate of formula (**10**) which is converted to (**I**) in the manner of Scheme **IV**.

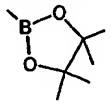
The desired intermediates of formula (**10**) of Scheme **IV** wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**) and **C** is (**d**), (**e**) or (**f**), or **B** is (**b**) and **C** is either (**c**), (**d**), (**e**) or (**f**), can be prepared in analogous fashion by replacing intermediates of formulas (**8** and **9**) with appropriately substituted naphthyl, quinolyl, pyrimidinyl or pyrazinyl intermediates.

The required appropriately substituted aryl(heteroaryl) halides of formula (**8**, M= Br or I) of Scheme **IV** are either available commercially, or are known in the art or can be readily accessed in quantitative yields and high purity by diazotization of the corresponding substituted anilines (**8**, *P*= H, alkyl or benzyl, M= NH_2) followed by reaction of the intermediate diazonium salt with iodine and potassium iodide in aqueous acidic medium essentially according to the procedures of Street et al,. *J. Med. Chem.* **36**, 1529 (1993) and Coffen et al., *J. Org. Chem.* **49**, 296 (1984) or with copper(I) bromide, respectively (March, *Advanced Organic Chemistry*, 3rd Edn., p.647-648, John Wiley & Sons, New York (1985)).

Alternatively, the desired intermediates of formula (**11**, A= CH) of Scheme **IV** wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**, A= CH) and **C** is (**c**, A= CH) can be conveniently prepared as shown in Scheme **V** by cross-coupling reaction of an appropriately substituted pinacolato borane of formula (**13**, A= CH) wherein R_8, R_9 and R_{10} are hereinbefore defined, with an aryl triflate of formula (**14**, Y= OTf) or an aryl halide (**14**, Y= Br, I) wherein R_5, R_6 and R_7 are defined hereinbefore, according to the general procedures of Ishiyama et al., *Tetr. Lett.* **38**, 3447-3450 (1997) and Giroux et al. *Tetr. Lett.* **38**, 3841-3844 (1997), followed by basic or acidic hydrolysis of the intermediate nitrile of formula (**15**) (cf. March, *Advanced Organic Chemistry*, 3rd Edn., John Wiley & Sons, New York, p. 788 (1985)).

Scheme V



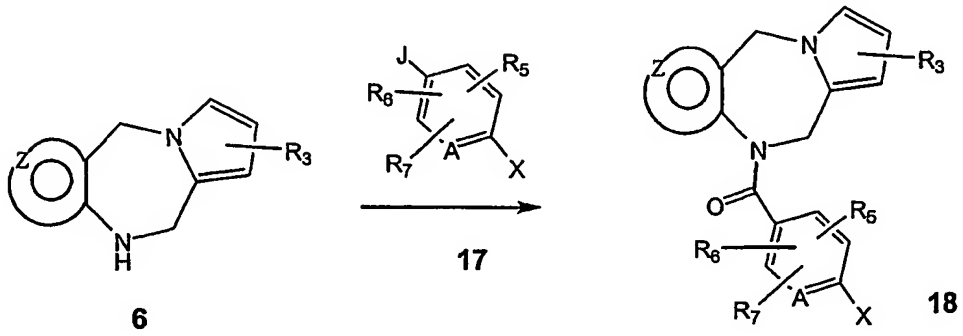
Alternatively, reaction of an iodide (bromide, chloride, or trifluoromethanesulfonate) of formula (**12**, X= Br, Cl, I, or OTf) with a bis(pinacolato)diboron [boronic acid or trialkyl tin(IV)] derivative of formula (**14**, Y=  , $B(OH)_2$, or $SnBu_3$) yields the desired intermediate of formula (**15**) which is converted to (**11**) in the manner of Scheme **V**.

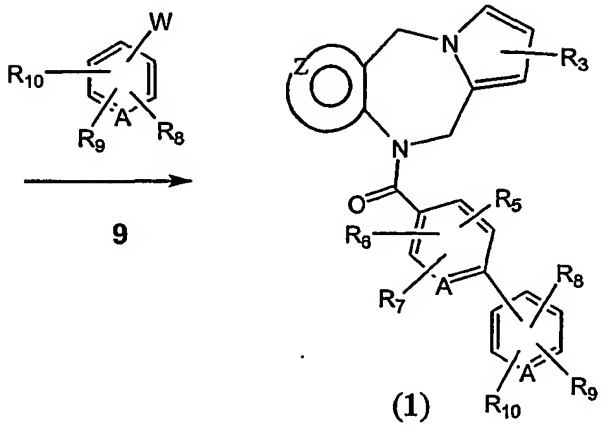
The desired intermediates of formula (**11**) of Scheme **IV** can be prepared in analogous fashion by replacing intermediates of formulas (**13** and **14**) with appropriately substituted naphthyl intermediates.

The desired phenyl boronic esters of formula (**13**) of Scheme **V** can be conveniently prepared by the palladium-catalyzed cross-coupling reaction of the pinacol ester of diboronic acid (**16**) with an appropriately substituted aryl halide preferably a bromide or iodide (**12**, X= Br, I) or aryl triflate (**12**, X= OTf) according to the described procedures of Ishiyama et al., *J. Org. Chem.* **60**, 7508-7510 (1995) and Giroux et al., *Tetr. Lett.* **38**, 3841-3844 (1997).

The desired compounds of formula (**1**) of Scheme **IV** wherein R_4 consists of the moiety **B-C** wherein **B** is (a) and **C** is (c) can be alternatively prepared by a process shown in Scheme **VI.**

Scheme VI





Thus, a tricyclic diazepine of formula (**6**) is treated with an appropriately substituted acylating agent such as a halo aroyl(heteroaroyl)halide, preferably an iodo(bromo) aroyl(heteroaroyl) chloride(bromide) of formula (**17**, J= COCl or COBr; X= I, Br) wherein A, R_5, R_6 and R_7 are hereinbefore defined using any of the procedures hereinbefore described, to provide the acylated intermediate of general formula (**18**) of Scheme **VI.**

Alternatively, the acylating species of formula (**17**) can be a mixed anhydride of the corresponding carboxylic acid. Treatment of said mixed anhydride of general formula (**17**) with a tricyclic diazepine of formula (**6**) according to the procedure described hereinbefore yields the intermediate acylated derivative (**18**).

The acylating intermediate of formula (**17**) is ultimately chosen on the basis of its compatibility with A and the R_5, R_6 and R_7 groups, and its reactivity with the tricyclic diazepine of formula (**6**).

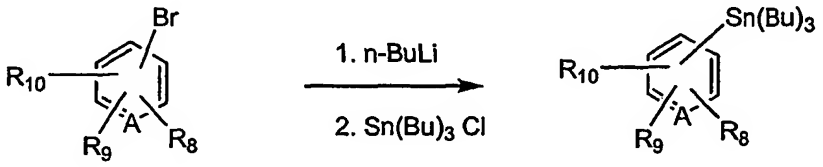
A Stille coupling reaction of (**18**, X= I) with an appropriately substituted organotin reagent such as a trialkyltin(IV) derivative, preferably a tri-*n*-butyltin(IV) derivative of formula (**9**, W= $SnBu_3$) where A, R_8, R_9 and R_{10} are hereinbefore defined, in the presence of a catalyst such as tetrakis (triphenylphosphine) palladium (0) in an aprotic organic solvent such as toluene and N,N-dimethylformamide, at temperatures ranging from ambient to 150°C (cf. Farina et al., *J. Org. Chem,* **59**, 5905 (1994) and references cited therein) affords the desired compounds of formula (**1**) wherein  , A, R_3, R_5, R_6, R_7, R_8, R_9 and R_{10} are as defined hereinbefore.

Alternatively, the reaction of a compound of formula (**18**, X= Cl, Br or I) with an appropriately substituted aryl(heteroaryl) boronic acid of formula (**9**, W= $B(OH)_2$) wherein A, R_5, R_6, R_7, R_8, R_9 and R_{10} are hereinbefore defined, in a mixture of solvents such as toluene-ethanol-water, and in the presence of a Pd(0) catalyst and a base such as sodium carbonate, at temperatures ranging from ambient to the reflux temperature of the solvent, yields the desired compounds of formula (**1**) wherein  , A, R_3, R_5, R_6, R_7, R_8, R_9 and R_{10} are as defined hereinbefore.

The preferred substituted aroyl(heteroaroyl) chlorides(bromides) of formula (**17**) of Scheme **VI** (X= I, Br; J= COCl or COBr) wherein A, R_5, R_6 and R_7 are as defined hereinbefore, are either available commercially, or are known in the art, or can be readily prepared by procedures analogous to those in the literature for the known compounds.

The intermediates of formula (**9**, W= Sn(alkyl)$_3$, alkyl= *n*-butyl) of Scheme **VI** are either commercially available, or can be conveniently prepared as shown in Scheme **VII** from the corresponding bromo starting materials of formula (**20**) wherein A, R_8, R_9, and R_{10} are hereinbefore defined, by first reacting them with *n*-butyl lithium followed by reaction of the intermediate lithiated species with a trialkyl (preferably trimethyl or tri-*n*-butyl)tin(IV) chloride.

Scheme VII



20 **9**

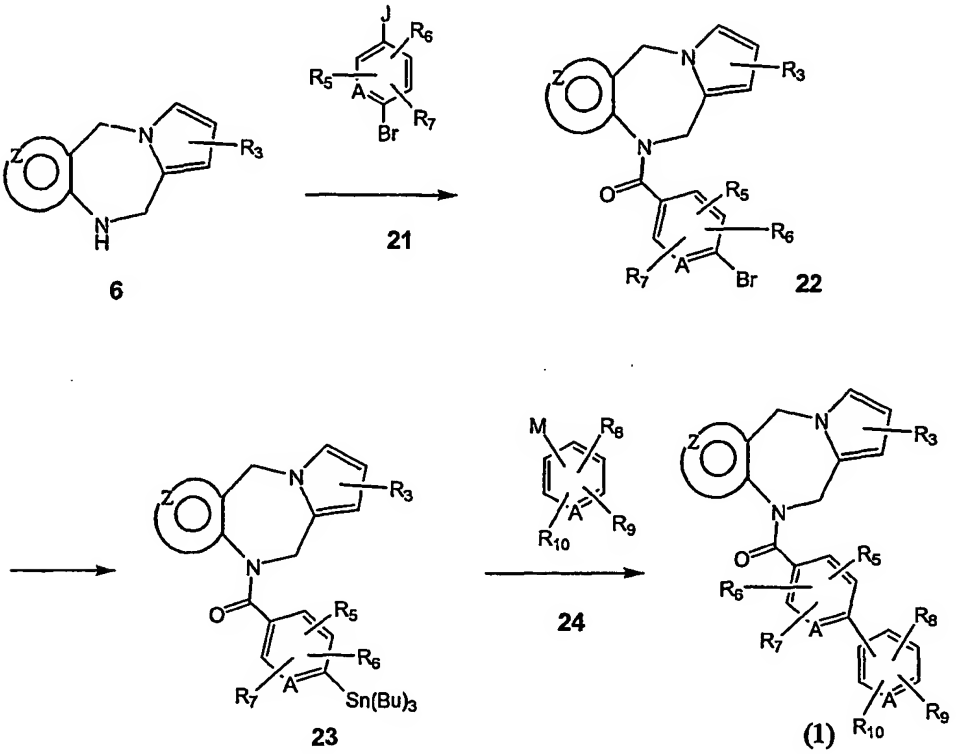
The preferred substituted aryl(heteroaryl) boronic acids of formula (**9**, W= B(OH)$_2$) are either available commercially, or are known in the art, or can be readily prepared by procedures analogous to those in the literature for the known compounds.

The desired compounds of formula (**1**) of Scheme **VI** wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**) and **C** is (**d**), (**e**) or (**f**), or **B** is (**b**) and **C** is either (**c**), (**d**), (**e**) or (**f**) can be prepared in analogous fashion by replacing intermediates of formulas (**17** and **9**) with appropriately substituted naphthyl, quinolyl, pyrimidinyl or pyrazinyl intermediates.

Alternatively, as shown in Scheme **VIII**, the appropriately substituted aroyl(heteroaroyl) halides, preferably aroyl(heteroaroyl) chlorides of formula (**21**, J= COCl) where A, R_5, R_6 and R_7 are hereinbefore defined, are reacted with a tricyclic diazepine of formula (**6**) to provide the intermediate bromides of formula (**22**). Subsequent reaction of (**22**) with an hexa alkyl-di-tin (preferably hexa-*n*-butyl-di-tin(IV)) in the presence of a Pd(0) catalyst such as tetrakis(tri-phenylphosphine)palladium(0) and lithium chloride, provides the stannane intermediate of formula (**23**). Further reaction of the tri-*n*-butyl tin(IV) derivative (**23**) with the appropriately substituted aryl(heteroaryl)

halide of formula (**24**, M = bromo or iodo) wherein A, R_8, R_9, and R_{10} are hereinbefore defined, in the presence of a Pd(0) catalyst such as tetrakis(triphenylphosphine) palladium(0), yields the desired compounds of formula (**1**) wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**) and **C** is (**c**), and  , A, R_5, R_6, R_7, R_8, R_9 and R_{10} are defined hereinbefore.

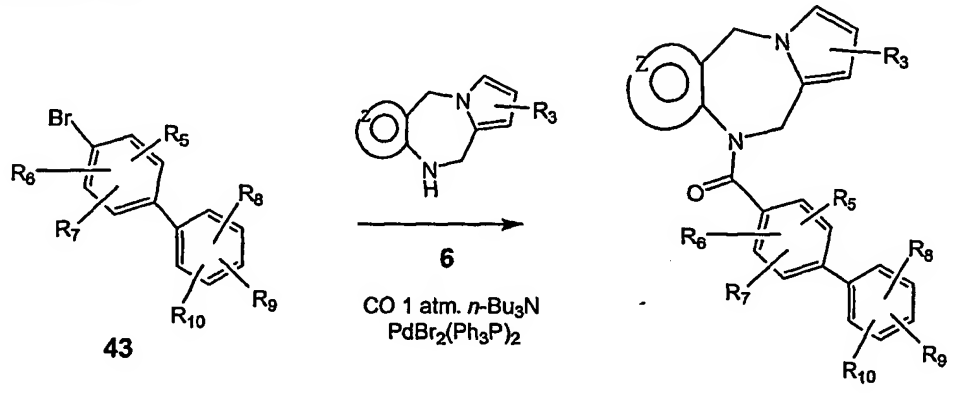
Scheme VIII



The desired compounds of formula (**1**) of Scheme **VIII** wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**) or (**b**) and **C** is (**d**), (**e**) or (**f**) can be prepared in analogous fashion by replacing intermediates of formulas (**21** and **24**) with appropriately substituted naphthyl, quinolyl, pyrimidinyl or pyrazinyl intermediates.

Alternatively, the desired compounds of formula (**1**) of Scheme **VIII** wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**, A= CH), and **C** is (**c**, A= CH) can be prepared as shown in Scheme **IX**.

Scheme IX

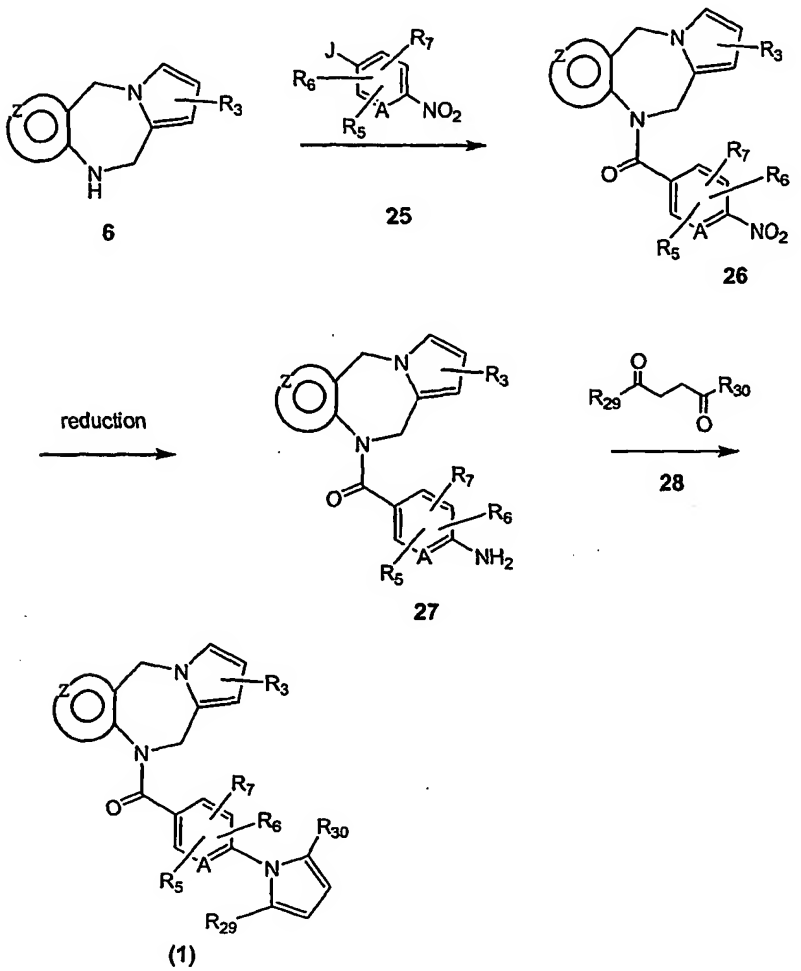


Thus, an appropriately substituted biphenyl of formula (**43**) wherein R_5, R_6, R_7, R_8, R_9 and R_{10} are defined hereinbefore, is treated with carbon monoxide in the presence of a tricyclic diazepine of formula (**6**), a palladium(0) catalyst preferably $PdBr_2(Ph_3P)_2$ and a tertiary amine preferably n-tributylamine, in a solvent such as anisole or dioxane at temperatures ranging from ambient to the reflux temperature of the solvent (cf. Schoenberg et al., *J. Org. Chem.* **39**, 3327 (1974)) to provide the desired compounds of formula (**1**) wherein A is CH, and  , R_3, R_5, R_6, R_7, R_8, R_9 and R_{10} are defined hereinbefore.

In analogous fashion one can prepare compounds of formula (**1**) of Scheme **IX** wherein R_4 consists of the moiety **B-C** wherein **B** is (**b**) and **C** is (**c**, A= CH) or (**d**, A= CH) provided that the intermediates of formula (**43**) are replaced by the appropriately substituted phenyl or naphthyl intermediates.

A preferred process for the preparation of the compounds of formula (**1**) of Scheme **I** wherein  , A, R_3, R_5, R_6 and R_7 are defined hereinbefore, R_4 consists of the moiety **B-C** wherein **B** is (**a**) and **C** is (**g**) defined hereinbefore, is shown in Scheme **X**.

Scheme X



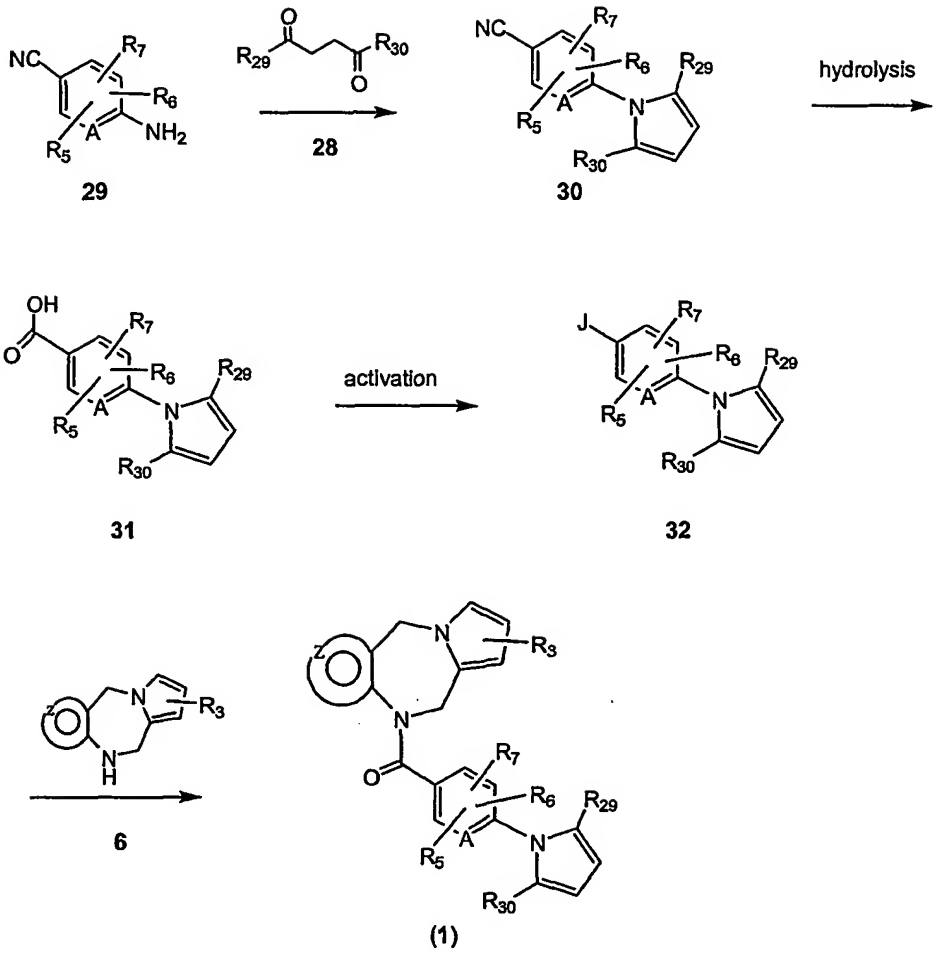
Thus, an appropriately substituted aroyl(heteroaroyl) halide preferably an aroyl(heteroaroyl) chloride, of formula (**25**, J= COCl) is reacted with a tricyclic diazepine of formula (**6**) in the presence of a base such as pyridine, or a tertiary amine such as triethylamine or N,N-diisopropylethyl amine, in an aprotic organic solvent such as dichloromethane or tetrahydrofuran, at temperatures from -40°C to 50°C to provide the acylated intermediate of formula (**26**). Alternatively, the acylating species can be a mixed anhydride under the reaction conditions described hereinbefore. Subsequent reduction

of (**26**) is preferably effected under conditions of catalytic reduction (i.e. hydrogen, Pd on charcoal), transfer hydrogenation (i.e. hydrazine/ ethanol/ Pd on charcoal) or under chemical reduction conditions (i.e. with tin(II)chloride dihydrate in a protic organic solvent such as ethanol, or zinc in acetic acid) or related reduction conditions known in the art, to yield the desired aniline of formula (**27**). The exact conditions for the conversion of the nitro to amino group are chosen on the basis of compatibility with the preservation of other functional groups in the molecule. Condensation of (**27**) with a 1,4-diketone of formula (**28**) in an aprotic organic solvent such as benzene or toluene in the presence of acetic acid or a catalytic amount of p-toluene sulfonic acid with concomitant removal of water at temperatures ranging from ambient to reflux temperature of the solvent according to the general procedure of Bruekelman et al., *J. Chem. Soc. Perkin Trans. I*, 2801-2807 (1984), provides the desired compounds of formula (**1**) wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**) and **C** is (**g**), and  , A, R_3, R_5, R_6, R_7, R_{29} and R_{30} are defined hereinbefore.

The desired compounds of formula (**1**) of Scheme **X** wherein R_4 consists of the moiety **B-C** wherein **B** is (**b**) and **C** is (**g**) can be prepared in analogous fashion by replacing the intermediate of formula (**25**) with an appropriately substituted naphthyl.

Alternatively, the desired compounds of formula (**1**) of Scheme **X** can be prepared as shown in Scheme **XI.**

Scheme XI



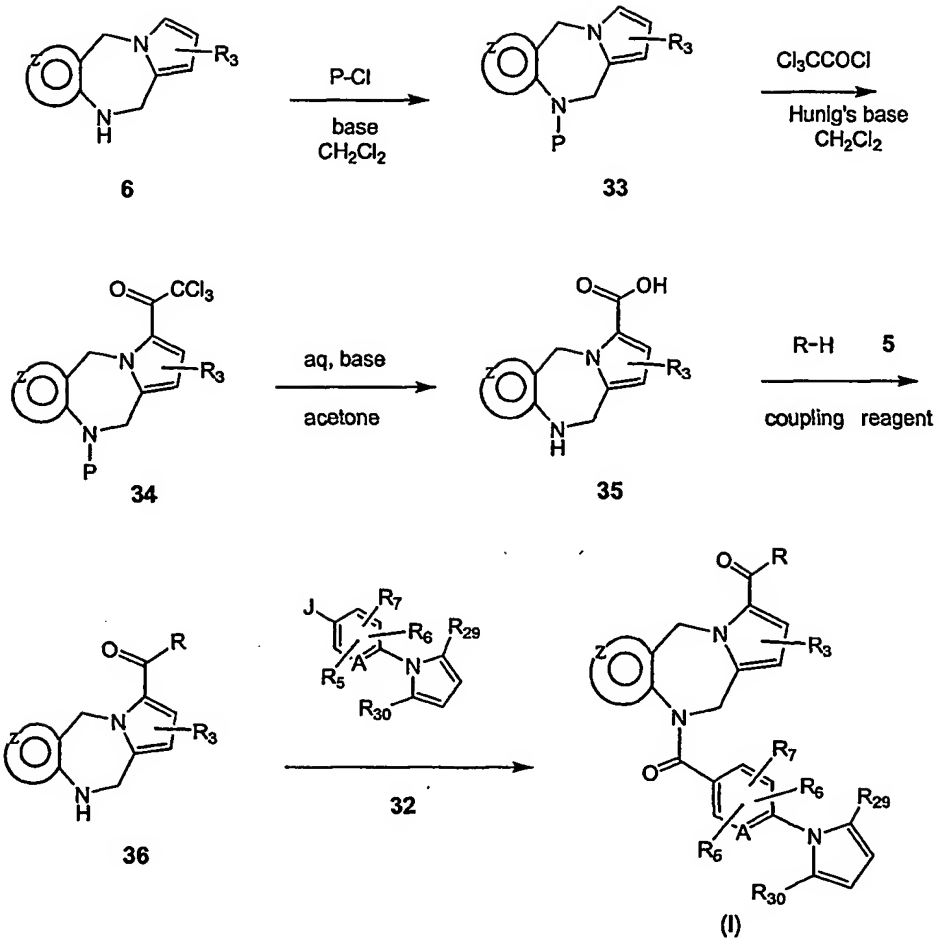
According to this process an aryl(heteroaryl) nitrile of formula (**29**) is condensed with a 1,4-diketone of formula (**28**) in an aprotic organic solvent such as benzene or toluene, in the presence of acetic acid or a catalytic amount of p-toluenesulfonic acid with concomitant removal of water, at temperatures ranging from ambient to reflux temperature of the solvent according to the general procedure of Bruekelman et al., *J. Chem. Soc. Perkin Trans. I*, 2801-2807 (1984), to yield the intermediate pyrrole of formula (**30**). Subsequent hydrolysis of the nitrile (**30**) to the carboxylic acid of formula (**31**) is efficiently accomplished by treatment of (**30**) with aqueous base (cf. March, *Advanced Organic Chemistry*, 3rd Edn., John Wiley & Sons, New York, p. 788 (1985)). Subsequent conversion of the acid (**31**) into an acylating species, preferably an acid chloride(bromide) of formula (**32**, J= COCl or COBr) or a mixed anhydride is

accomplished by procedures analogous to those described hereinbefore. The acylating agent (**32**) is used to acylate a tricyclic diazepine of formula (**6**) to provide the desired compounds of formula (**1**) wherein  , A and R_3 are defined hereinbefore, and R_4 consists of the moiety **B-C** wherein **B** is (**a**) and **C** is the moiety (**g**) defined hereinbefore.

The compounds of formula (**1**) of Scheme **XI** wherein R_4 consists of the moiety **B-C** wherein **B** is (**b**) and **C** is (**g**) defined hereinbefore can be prepared in analogous fashion by replacing the intermediates of formula (**29**) with an appropriately substituted naphthyl.

A preferred process for the preparation of the desired compounds of general formula (**I**) of Scheme **I** wherein R_4 consists of the moiety **B-C**, where **B** is selected from the group (**a**) and **C** is selected from the group (**g**) defined hereinbefore is shown in Scheme **XII**.

Scheme XII



Thus, a tricyclic diazepine of formula (**33**) wherein  and R_3 are defined hereinbefore, carrying a protecting group such as a fluorenylalkoxycarbonyl group, preferably a fluorenylmethyloxycarbonyl (*P*= Fmoc) group, or an alkoxycarbonyl protecting group preferably a tert-butyloxycarbonyl (*P*= Boc) group is reacted with a perhaloalkanoyl halide preferably trichloroacetyl chloride in the presence of an organic base such as N,N-diisopropylethyl amine (Hünig's base) or a tertiary amine such as triethylamine, optionally in the presence of catalytic amounts of 4-(dimethylamino)-pyridine, in an aprotic organic solvent such as dichloromethane, at temperatures ranging from -10°C to ambient to provide the desired trichloroacetyl intermediate of formula (**34**). Subsequent hydrolysis of the trichloroacetyl group with aqueous base such as sodium

hydroxide in an organic solvent such as acetone at temperatures ranging from -10°C to ambient, is accompanied by simultaneous removal of the protecting group and yields the intermediate acid of formula (**35**). The required amidation of the carboxylic acid (**35**) can be effectively accomplished by treating (**35**) with an activating reagent such as N,N-dicyclohexylcarbodiimide or 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride in the presence of 1-hydroxybenzotriazole, followed by reaction of the activated intermediate with an appropriately substituted primary or secondary amine of formula (**5**) preferably in the presence of Hünig's base or a catalytic amount of 4-(dimethylamino)pyridine, in an aprotic solvent such as dichloromethane, N,N-dimethylformamide or tetrahydrofuran, at temperatures ranging from -10°C to ambient.

Other coupling reagents known in the literature that have been used in the formation of amide bonds in peptide synthesis can also be used for the preparation of compounds of formula (**36**) wherein  , R and R_3 are as defined hereinbefore. The method of choice for the preparation of compounds of formula (**36**) from the intermediate carboxylic acid (**35**) is ultimately chosen on the basis of its compatibility with the various substituents, and its reactivity with the tricyclic diazepine of formula (**6**). Subsequent reaction of a tricyclic diazepine amide (**36**) with an acylating agent of formula (**32**) of Scheme **XI** provides the desired compounds of formula (**I**) wherein  , A and R_3 are defined hereinbefore, R_4 consists of the moiety **B-C** wherein **B** is (**a**) and **C** is the moiety (**g**) defined hereinbefore.

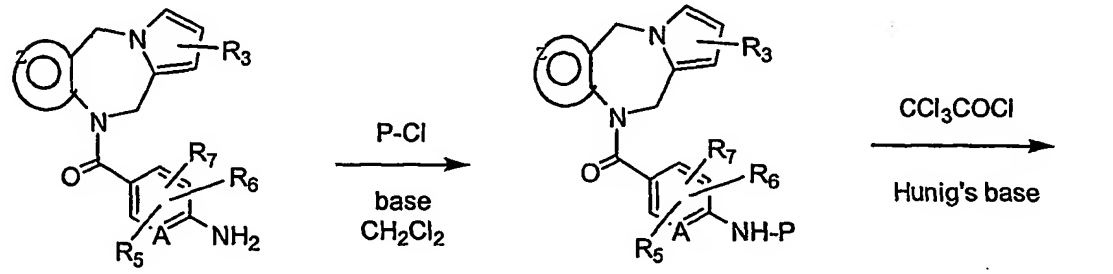
The preferred compounds of formula (**I**) of Scheme **I** wherein R_4 consists of the moiety **B-C** wherein **B** is (**b**) and **C** is the moiety (**g**) defined hereinbefore, can be prepared in analogous fashion by replacing the intermediate of formula (**32**) of Scheme **XII** with an appropriately substituted naphthyl intermediate.

Preferred processes for the preparation of compounds of formula (**I**) of Scheme **I** wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**) or (**b**) and **C** is (**d**), (**e**) or (**f**) and  , A, R, R_3, R_5, R_6, R_7, R_8, R_9, and R_{10} are defined hereinbefore, also utilize acylation

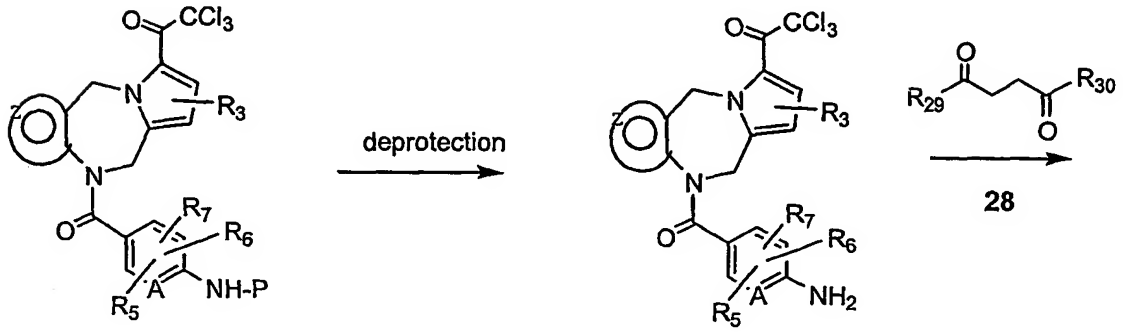
of the amide intermediate (**36**) of Scheme **XII** with an acylating agent of formula (**19**) of Scheme **IV**.

An alternate preferred process for the preparation of the compounds of formula (**I**) of Scheme **I** wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**) and **C** is (**g**) defined hereinbefore, is shown in Scheme **XIII**.

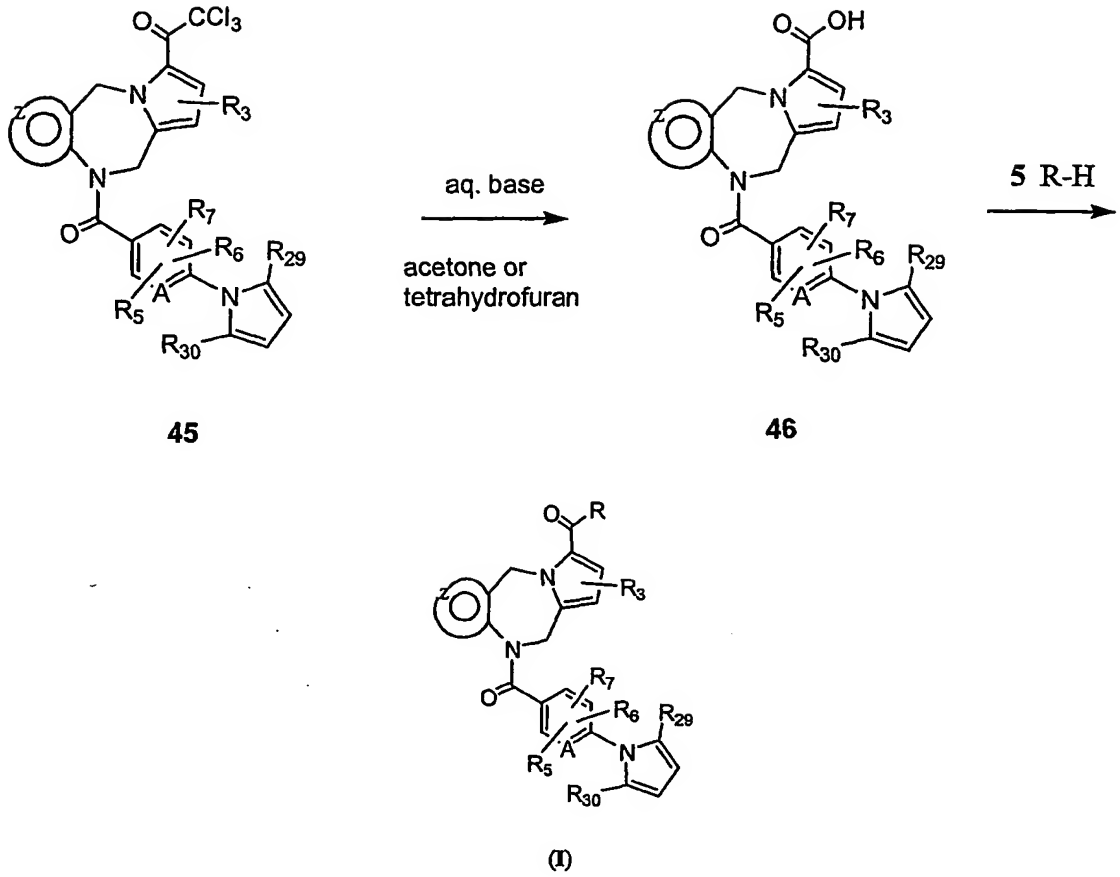
Scheme XIII



27 **37**



38 **44**



45 46

(I)

According to the above process a substituted tricyclic diazepine of formula (**37**) wherein  , A, R_3, R_5, R_6 and R_7 and are defined hereinbefore, carrying a protecting group such as a fluorenylalkoxycarbonyl group, preferably a fluorenylmethyloxycarbonyl (*P*= Fmoc) group is reacted with a perhaloalkanoyl halide preferably trichloroacetyl chloride in the presence of an organic base such as N,N-diisopropylethyl amine (Hünig's base) or a tertiary amine such as triethylamine in an aprotic organic solvent such as dichloromethane at temperatures ranging from –10 °C to ambient, to provide the desired trichloroacetyl intermediate of formula (**38**). Subsequent deprotection of (**38**) is carried out by treatment with a solution of an organic base preferably piperidine, in an organic solvent such as N,N-dimethylformamide, at ambient temperature to provide the desired aniline (**44**). Condensation of (**44**) with a 1,4-diketone of formula (**28**) either neat or in an aprotic organic solvent such as benzene or toluene, in the presence of a catalytic

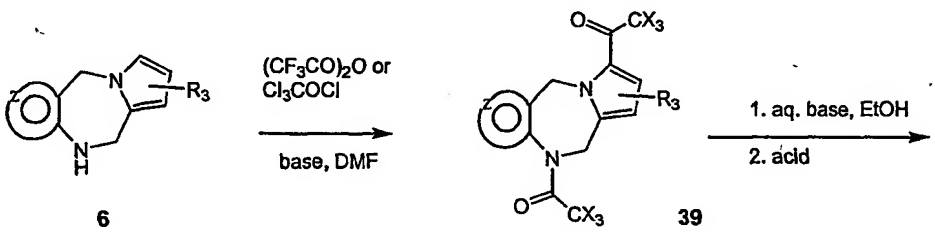
amount of a carboxylic acid preferably p-toluene sulfonic acid or acetic acid , with concomitant removal of water, at temperatures ranging from ambient to 100 °C or to the reflux temperature of the solvent according to the general procedure of Bruekelman et al., *J. Chem. Soc. Perkin Trans. I*, 2801-2807 (1984), provides the desired intermediate of formula (**45**). Subsequent hydrolysis of the trichloroacetyl group with aqueous base such as sodium hydroxide, in an organic solvent such as acetone or tetrahydrofuran, at temperatures ranging from -10°C to the reflux temperature of the solvent, yields the intermediate carboxylic acid of formula (**46**). Subsequent amidation provides the desired compounds of formula (**I**) wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**) and **C** is (**g**), and  , A, R_3, R_5, R_6, R_7, R_{29} and R_{30} are defined hereinbefore,

The required amidation of (**46**) can be effectively accomplished by treating said carboxylic acid with an activating reagent such as N,N-dicyclohexylcarbodiimide or 1-ethyl-3-(3-dimethylamino-propyl) carbodiimide hydrochloride in the presence of 1-hydroxybenzotriazole, followed by reaction of the activated intermediate with an appropriately substituted primary or secondary amine of formula (**5**) preferably in the presence of Hünig's base or a catalytic amount of 4-(dimethylamino)pyridine, in an aprotic solvent such as dichloromethane, N,N-dimethylformamide or tetrahydrofuran, at temperatures ranging from -10°C to ambient. Other coupling reagents known in the literature that have been used in the formation of amide bonds in peptide synthesis can also be used for the preparation of compounds of formula (**I**) wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**) and **C** is (**g**), and  , A, R_3, R_5, R_6, R_7, R_{29} and R_{30} are defined hereinbefore. The method of choice for the preparation of compounds of formula (**I**) from the intermediate carboxylic acid (**46**) is ultimately chosen on the basis of its compatibility with the  and R_3 groups, and its reactivity with the tricyclic diazepine of formula (**6**).

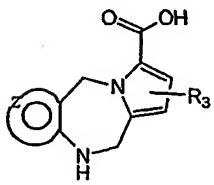
The desired compounds of formula (**I**) of Scheme **XIII** wherein R_4 consists of the moiety **B-C** wherein **B** is (**b**) and **C** is (**g**) can be prepared in analogous fashion by replacing the intermediate of formula (**27**) with an appropriately substituted naphthyl intermediate.

Alternatively, the intermediate acids of formula (**35**) of Scheme **XII** wherein  and R_3 are defined hereinbefore, can be obtained by reacting a tricyclic diazepine of formula (**6**) with an excess of acylating agent preferably trifluoroacetic anhydride or trichloroacetyl chloride in the presence of an inorganic base such as potassium carbonate or an organic base such as N,N-diisopropylethyl amine, in an aprotic solvent such as N,N-dimethylformamide, followed by basic hydrolysis of the intermediate bis-trifluoroacetyl (trichloroacetyl) intermediate of formula (**39** X= F or Cl), preferably with aqueous sodium hydroxide in a protic organic solvent such as ethanol, at temperatures ranging from ambient to the reflux temperature of the solvent as exemplified in Scheme **XIV**.

Scheme XIV



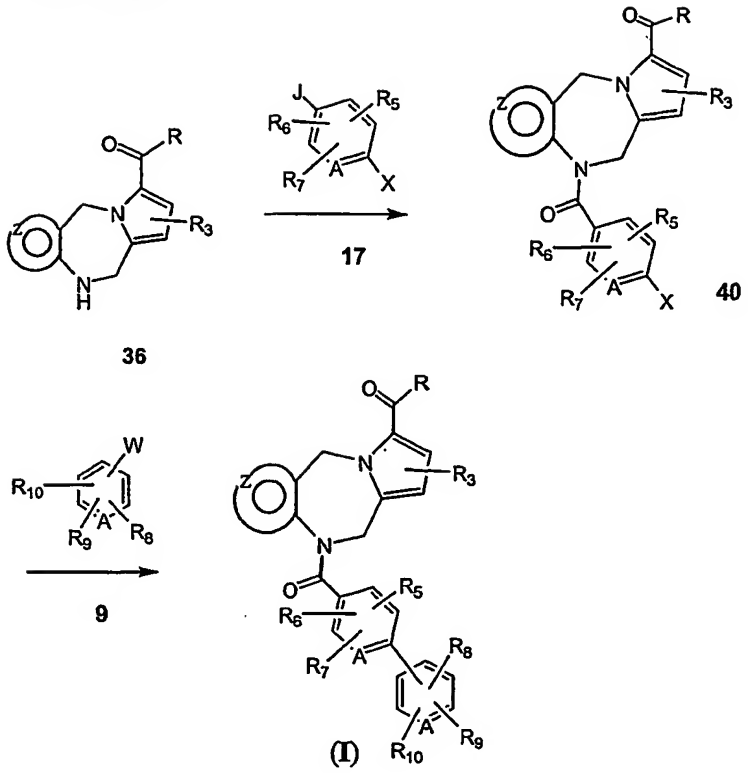
6 **39**



35

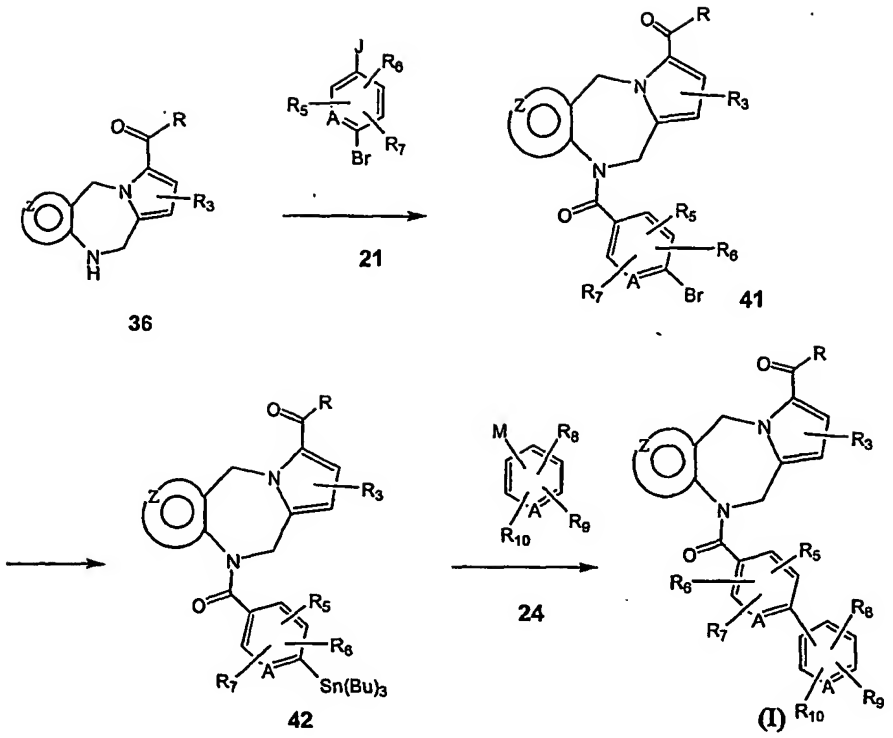
Preferred processes for the preparation of compounds of formula (**I**) of Scheme **I** wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**) or (**b**) and **C** is (**d**), (**e**) or (**f**) and  , A, R, R_3, R_5, R_6, R_7, R_8, R_9, and R_{10} are defined hereinbefore, also utilize acylation of the amide intermediate (**36**) of Scheme **XII** with an acylating agent of formula (**17**) of Scheme **IV**, as shown in Scheme **XV**.

Scheme XV



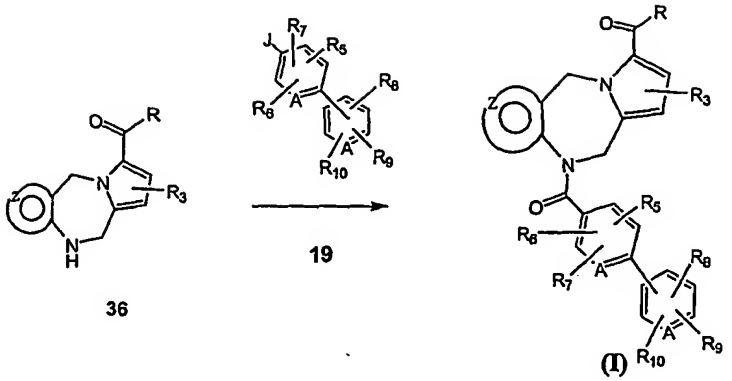
Alternatively, the preferred compounds of formula (I) of Scheme I wherein R_4 consists of the moiety **B-C** wherein **B** is (a) and **C** is (c) and  , A, R, R_3, R_5, R_6, R_7, R_8, R_9, and R_{10} are defined hereinbefore, can be prepared by acylation of the amide intermediate (**36**) of Scheme **XII** with an acylating agent of formula (**21**) of Scheme **VIII**, as shown in Scheme **XVI**.

Scheme XVI



Alternatively, the preferred compounds of formula (I) of Scheme (I) wherein R_4 consists of the moiety **B-C** wherein **B** is (**a**) and **C** is (**c**) and  , A, R, R_3, R_5, R_6, R_7, R_8, R_9, and R_{10} are defined hereinbefore, can be prepared by acylation of the amide intermediate (**36**) of Scheme **XII** with an acylating agent of formula (**19**) of Scheme **IV**, wherein J is hereinbefore defined, as shown in Scheme **XVII**.

Scheme XVII



The subject compounds of the present invention were tested for biological activity according to the following procedures.

Vasopressin binding in Chinese Hamster Ovary cell membranes expressing human vasopressin V_{1a} subtype receptors

Receptor source:

Chinese hamster ovary cells (CHO cells) stably transfected with the human vasopressin V_{1a} subtype receptors were either obtained from BioSignal Inc., 1744 rue Williams, Montreal, Quebec, Canada or obtained from M. Thibonnier, Case Western Reserve University School of Medicine, Cleveland, OH.

A. Passaging and Amplification of Cells:

CHO cells transfected with the human vasopressin V_{1a} subtype receptors obtained from M. Thibonnier (pZeoSV vector) are allowed to grow to confluency (approx. >90%) in T-150 flasks under sterile conditions, in a cell culture medium of F-12 Nutrient Mixture (HAM) with L-glutamine (Gibco Cat. # 11765-054) containing 15 mM HEPES (Gibco Cat. # 15630-080), 1% antibiotic/ antimycotic (add 5 mL 100x, Gibco Cat. # 15240-062 per 500 mL F-12), 250 µg/mL Zeocin (add 1.25 mL of 100 mg/mL Invitrogen R-250-01 per 500 mL F-12) and 10% Fetal Bovine Serum (Qualified, heat inactivated, Gibco Cat. # 16140-063). The medium is removed by aspiration and the cells are washed with 10 mL of Hank's Balanced Salt solution (Gibco Cat. # 14175-095). The salt solution is removed by aspiration and the cells are trypsinized with 5 mL of trypsin-EDTA (0.05% trypsin,

0.53 mM EDTA-4Na, Gibco Cat. # 25300-070) for 1 min. The trypsin is removed by aspiration and the cells dislodged by tapping. Cell Culture medium (e.g. 30 mL for 1:30 split) is immediately added and mixed well to inactivate trypsin. 1 mL of detached cells is added to new culture flasks containing fresh cell culture medium (e.g., into 25 mL per T-150 flask), and mixed gently. The cells are incubated at 37 °C in 5% CO_2. The medium is changed at 3 to 4 days interval (or as appropriate). The cells grow to confluency (approx. >75%-95%) within 7-8 days. All steps are done under sterile conditions.

B. Membrane Preparation:

The cells are washed twice gently with Hank's Balanced Salt solution (e.g,. use 10 mL per T-150 flask). The excess is removed and the cells are bathed for 15-30 min. in an enzyme-free Cell Dissociation Buffer (e.g. use 8 mL Hank's Based, Gibco Cat. # 13150-016 per T-150 flask) until the cells are loosened. The contents are transferred to centrifuge tubes (50 mL) kept in an ice bath. All subsequent steps are done at 4 °C. The tubes are centrifuged at 300 x g for 15 min (1380 rpm on SORVAL, Model RT6000D, using the rotor for 50 mL tubes). The supernatant is discarded and the cells suspended in homogenizing buffer(10 mM Tris-HCl containing 0.25 M sucrose and 1 mM EDTA, pH 7.4) ensuring that the volume of the buffer is about ten times the volume of the cell pellet. The cells are pooled into a centrifuge tube (50 mL) and homogenized with a Polytron at setting 6 for 10 sec. The homogenate is transferred into a Potter-Elvjehm homogenizer and homogenized with 3 strokes. The homogenate is centrifuged at 1500 x g for 10 min at 4°C (3100 rpm using SORVAL, model RT6000D, using the rotor for 50 mL tubes). The pellet is discarded. The supernatant is centrifuged at 100,000 x g for 60 min. at 4 °C (Beckman L8-80M ultracentrifuge; spin at 37,500 rpm with rotor type 70 Ti for 50 mL tubes; 38,000 rpm with type 80Ti for 15 mL tubes; or 35,800 rpm with rotor type 45Ti). The supernantant is discarded and the pellet suspended in 3 to 4 mL of Tris buffer (50 mM TRIS-HCl, pH 7.4). The protein content is estimated by the Bradford or Lowry method. The volume of the membrane suspension is adjusted with the membrane buffer (50 mM Tris-HCl containing 0.1% BSA and 0.1 mM PMSF) to give 3.0 mg/mL (or as appropriate) of protein. The membranes are aliquoted and stored at -70 °C.

C. Radioligand Binding Assay:

In wells of a 96-well format microtiter plate, is added 90, 110 or 130 µL (to make up a final volume of 200 µL) of assay buffer containing 50 mM of Tris-HCl (pH 7.4), BSA (heat inactivated, protease-free), 0.1% of 5 mM $MgCl_2$, 1 mg% aprotinin, 1 mg% leupeptin, 2 mg% 1,10-phenanthroline, 10 mg% trypsin inhibitor, and 0.1 mM PMSF. The inhibitors are added on the day of the experiment. The components are mixed at room temperature, and then kept in ice bath following adjustment of the pH to 7.4.

To each well is added 20 µL of unlabeled Manning ligand (to give a final concentration of 0.1 to 10 nM for standard curve and 1000 nM for non specific binding) or test compounds in 50% DMSO (e.g. for final concentrations of 0.1 to 1000 nM or as appropriate) or 50% DMSO as vehicle control. 20 µL of 50% DMSO is added for Manning and other peptide ligands and the assay buffer volume is adjusted accordingly.

To each well is added 50 µL of frozen membrane suspension thawed immediately prior to use and diluted in the assay buffer to the required concentration (equivalent to 25 to 50 µg of protein/well as needed). 20 µL of 8 nM [^{3}H]Manning ligand in the assay buffer, prepared just before use, is added, and incubated at room temperature for 60 min. shaking the plate on a mechanical shaker for the first 15 min. The incubation is stopped by rapid filtration of the the plate contents followed by wash with ice-cold buffer (50 mM Tris-HCl, pH 7.4) using a cell harvester (Tomtek and Printed filtermat-B filter paper). The filter paper is thoroughly dried (7-12 min. in a microwave oven) and impregnated with MeltiLex B/H melt-on scintillation wax sheets and the radioactivity counted in a betaplate scintillation counter.

Vasopressin binding in Chinese Hamster Ovary cell membranes expressing human vasopressin V_2 subtype receptors

Receptor Source:

Chinese Hamster Ovary (CHO) cells stably transfected with the human V_2 subtype receptors were obtained from M. Thibonnier, Case Western Reserve University School of Medicine, Cleveland, OH.

A. Passaging and Amplification of Cells:

CHO cells transfected with the human vasopressin V_2 subtype receptors obtained from M. Thibonnier (pZeoSV vector) are allowed to grow to confluency (approx. >90%) in T-150 flasks under sterile conditions, in a cell culture medium of F-12 Nutrient Mixture (HAM) with L-glutamine (Gibco Cat. # 11765-054) containing 15 mM HEPES (Gibco Cat. # 15630-080), 1% antibiotic/ antimycotic (add 5 mL 100x, Gibco Cat. # 15240-062 per 500 mL F-12), 250 µg/mL Zeocin (add 1.25 mL of 100 mg/mL Invitrogen R-250-01 per 500 mL F-12) and 10% Fetal Bovine Serum (Qualified, heat inactivated, Gibco Cat. # 16140-063). The medium is removed by aspiration and the cells washed with 10 mL of Hank's Balanced Salt solution (Gibco Cat. # 14175-095). The salt solution is removed by aspiration and the cells trypsinized with 5 mL of trypsin-EDTA (0.05% trypsin, 0.53 mM EDTA-4Na, Gibco Cat. # 25300-070) for 1 min. The trypsin is removed by aspiration and the cells dislodged by tapping. Cell Culture medium (e.g. 30 mL for 1:30 split) is immediately added and mixed well to inactivate trypsin. 1 mL of detached cells is added to new culture flasks containing fresh Cell Culture medium (e.g. into 25 mL per T-150 flask), and mixed gently. The cells are incubated at 37 °C in 5% CO_2. The medium is changed at 3 to 4 day interval (or as appropriate). The cells grow to confluency (approx. >75%-95%) within 7-8 days. All steps are done under sterile conditions.

B. Membrane Preparation:

The cells are washed twice gently with Hank's Balanced Salt solution (e.g. use 10 mL per T-150 flask). The excess solution is removed and the cells bathed for 15-30 min. in an enzyme-free Cell Dissociation Buffer (e.g. use 8 mL Hank's Based, Gibco Cat. # 13150-016 per T-150 flask) until cells are loosened. The contents are transferred to centrifuge tubes (50 mL) kept in ice bath. All subsequent steps are done at 4°C. The tubes are centrifuged at 300 x g for 15 min (1380 rpm on SORVAL, Model RT6000D, using the rotor for 50 mL tubes). The supernatant is discarded and the cells suspended in homogenizing buffer (10 mM Tris-HCl containing 0.25 M sucrose and 1 mM EDTA, pH 7.4) ensuring that the volume of the buffer is about ten times the volume of the cell pellet. The cells are pooled into a centrifuge tube (50 mL) and homogenized with a Polytron at setting 6 for 10 sec. The homogenate is transferred into a Potter-Elvjehm homogenizer and homogenized with 3 strokes. The homogenate is centrifuged at 1500 x g for 60 min at 4°C (3100 rpm using SORVAL, model RT6000D, using the rotor for 50 mL tubes). The

pellet is discarded. The supernatant is centrifuged at 100,000 x g for 60 min. at 4 °C (Beckman L8-80M ultracentrifuge; spin at 37,500 rpm with rotor type 70 Ti for 50 mL tubes; 38,000 rpm with type 80Ti for 15 mL tubes; or 35,800 rpm with rotor type 45Ti). The supernantant is discarded and the pellet suspended in 3 to 4 mL of Tris buffer (50 mM TRIS-HCl, pH 7.4). The protein content is estimated by the Bradford or Lowry method. The volume of the membrane suspension is adjusted with the membrane buffer (50 mM Tris-HCl containing 0.1% BSA and 0.1 mM PMSF) to give 3.0 mg/mL (or as appropriate) of protein. The membranes are aliquoted and stored at -70 °C.

C. Radioligand Binding Assay:

In wells of a 96-well format microtiter plate, is added 90, 110 or 130 µL (to make up a final volume of 200 µL) of assay buffer containing 50 mM of Tris-HCl (pH 7.4), BSA (heat inactivated, protease-free), 5 mM of 0.1% $MgCl_2$, 1 mg% aprotinin, 1 mg% leupeptin, 2 mg% 1,10-phenanthroline, 10 mg% trypsin inhibitor, and 0.1 mM PMSF. The inhibitors are added on the day of the experiment. The components are mixed at room temperature, and then kept in ice bath following adjustment of the pH to 7.4.

To each well is added 20 µL of unlabeled arginine vasopressin (AVP) (to give a final concentration of 0.1 to 10 nM for standard curve and 1000 nM for non specific binding) or test compounds in 50% DMSO (e.g. for final concentrations of 0.1 to 1000 nM or as appropriate) or 50% DMSO as vehicle control. For vasopressin and other peptide ligands 20 µL of 50% DMSO is added and the assay buffer volume is adjusted accordingly.

To each well is added 50 µL of frozen membrane suspension thawed immediately prior to use and diluted in assay buffer to the required concentration (equivalent to 25 to 50 µg of protein/well as needed). 20 µL of 8 nM [^{3}H]arginine vasopressin ligand in the assay buffer, prepared just before use is added and incubated at room temperature for 60 min. shaking the plate on a mechanical shaker for the first 15 min. The incubation is stopped by rapid filtration of the plate contents followed by wash with ice-cold buffer (50 mM Tris-HCl, pH 7.4) using a cell harvester (Tomtek and Printed filtermat-B filter paper). The filter paper is thoroughly dried (7-12 min. in a microwave oven) and impregnated with MeltiLex B/H melt-on scintillation wax sheets and the radioactivity counted in a betaplate scintillation counter.

Oxytocin binding in Chinese Hamster Ovary cell membranes expressing human oxytocin receptors

Receptor Source:

Chinese Hamster Ovary (CHO) cells stably transfected with the human oxytocin receptor (cf. Tanizawa et al., U.S. Patent 5,466,584 (1995) to Rohto Pharmaceutical Co. Ltd., Osaka, Japan) were obtained from M. Thibonnier, Case Western Reserve University School of Medicine, Cleveland, OH.

A. Passaging and Amplification of Cells:

CHO cells transfected with the human oxytocin receptors obtained from M. Thibonnier (pcDNA3.1 vector) are allowed to grow to confluency (approx. >90%) in T-150 flasks under sterile conditions, in a cell culture medium of F-12 Nutrient Mixture (HAM) with L-glutamine (Gibco Cat. # 11765-054) containing 15 mM HEPES (Gibco Cat. # 15630-080), 1% antibiotic/ antimycotic (add 5 mL 100x, Gibco Cat. # 15240-062 per 500 mL F-12), 400 μg/mL of Geneticin (add 4 mL of 50 mg/mL per 500 mL F-12) and 10% Fetal Bovine Serum (Qualified, heat inactivated, Gibco Cat. # 16140-063). The medium is removed by aspiration and the cells are washed with 10 mL of Hank's Balanced Salt solution (Gibco Cat. # 14175-095). The salt solution is removed by aspiration and the cells trypsinized with 5 mL of trypsin-EDTA (0.05% trypsin, 0.53 mM EDTA-4Na, Gibco Cat. # 25300-070) for 1 min. The trypsin is removed by aspiration and the cells dislodged by tapping. Cell Culture medium (e.g. 30 mL for 1:30 split) is immediately added and mixed well to inactivate trypsin. 1 mL of detached cells is added to new culture flasks containing fresh Cell Culture medium (e.g. into 25 mL per T-150 flask), and mixed gently. The cells are incubated at 37 °C in 5% CO_2. The medium is changed at 3 to 4 days interval (or as appropriate). The cells grow to confluency (approx. >75%-95%) within 7-8 days. All steps are done under sterile conditions.

B. Membrane Preparation:

The cells are washed twice gently with Hank's Balanced Salt solution (e.g., use 10 mL per T-150 flask). The excess solution is removed and the cells bathed for 15-30 min. in an enzyme-free Cell Dissociation Buffer (e.g., use 8 mL Hank's Based, Gibco Cat. # 13150-016 per T-150 flask) until cells are loosened. The contents are transferred to

centrifuge tubes (50 mL size) kept in ice bath. All subsequent steps are done at 4°C. The tubes are centrifuged at 300 x g for 15 min (1380 rpm on SORVAL, Model RT6000D, using rotor for 50 mL tubes). The supernatant is discarded and the cells suspended in homogenizing buffer (10 mM Tris-HCl containing 0.25 M sucrose and 1 mM EDTA, pH 7.4) ensuring that the volume of the buffer is about ten times the volume of the cell pellet. The cells are pooled into a centrifuge tube (50 mL) and homogenized with a Polytron at setting 6 for 10 sec. The homogenate is transferred into a Potter-Elvjehm homogenizer and homogenized with 3 strokes. The homogenate is centrifuged at 1500 x g for 10 min at 4 °C (3100 rpm using SORVAL, model RT6000D, using rotor for 50 mL tubes). The pellet is discarded. The supernatant is centrifuged at 100,000 x g for 60 min. at 4°C (Beckman L8-80M ultracentrifuge; spin at 37,500 rpm with rotor type 70 Ti for 50 mL tubes; 38,000 rpm with type 80Ti for 15 mL tubes; or 35,800 rpm with rotor type 45Ti). The supernantant is discarded and the pellet suspended in 3 to 4 mL of Tris buffer (50 mM TRIS-HCl, pH 7.4). The protein content is estimated by the Bradford or Lowry method. The volume of the membrane suspension is adjusted with the membrane buffer (50 mM Tris-HCl containing 0.1% BSA and 0.1 mM PMSF) to give 3.0 mg/mL (or as appropriate) of protein. The membranes are aliquoted and stored at -70 °C.

C. Radioligand Binding Assay:

In wells of a 96-well format microtiter plate, is added 90, 110 or 130 µL (to make up a final volume of 200 µL) of assay buffer containing 50 mM of Tris-HCl (pH 7.4), BSA (heat inactivated, protease-free), 5 mM of 0.1% $MgCl_2$, 1 mg% aprotinin, 1 mg% leupeptin, 2 mg% 1,10-phenanthroline, 10 mg% trypsin inhibitor, and 0.1 mM PMSF. The inhibitors are added on the day of the experiment. The components are mixed at room temperature, and then kept in ice bath following adjustment of the pH to 7.4.

To each well is added 20 µL of unlabeled oxytocin (to give a final concentration of 0.1 to 10 nM for standard curve and 1000 nM for non specific binding) or test compounds in 50% DMSO (e.g. for final concentrations of 0.1 to 1000 nM or as appropriate) or 50% DMSO as vehicle control. For oxytocin and other peptide ligands, 20 µL of 50% DMSO is added and the assay buffer volume is adjusted accordingly.

To each well is added 50 µL of frozen membrane suspension thawed immediately prior to use and diluted in assay buffer to the required concentration (equivalent to 25 to 50 µg

of protein/well as needed). 20 µL of 8 nM [^{3}H]oxytocin in the assay buffer, prepared just before use is added and incubated at room temperature for 60 min. shaking the plate on a mechanical shaker for the first 15 min. The incubation is stopped by rapid filtration of the plate contents followed by washing with ice-cold buffer (50 mM Tris-HCl, pH 7.4) using a cell harvester (Tomtek and Printed filtermat-B filter paper). The filter paper is thoroughly dried (7-12 min. in a microwave oven) and impregnated with MeltiLex B/H melt-on scintillation wax sheets and the radioactivity counted in a betaplate scintillation counter.

Binding data is either reported as percent inhibition at a certain concentration or if an IC_{50} was calculated, as a nanomolar concentration.

The results of these tests on representative compounds of this invention are shown in Table I.

Table 1

Binding to membranes of Chinese Hamster Ovary (CHO) cell line stably transfected with human vasopressin V_{1a} receptor subtype, human vasopressin V_2 receptor subtype and human oxytocin receptor

Example	OT % inhibition @ 100 nM (IC_{50}, nM)*	V_{1a} % inhibition @ 100 nM (IC_{50}, nM)*	V_2 % inhibition @ 100 nM (IC_{50}, nM)*
2	(12.46)	(2718.5)	(1759.2)
3	37	-8	22
4	(8.89)	14	24
5	24	-6	3
6	56	2	13
7	(11.4)	(2481.3)	(2459.18)
8	(6.37)	(1370)	(1475)
9	32	10	42
11	(3.44)	(70.41)	(1351)
12	21	-10	-1
13	33	4	-4
14	9	-16	-3
15	-4	-8	27
17	28	-11	32
18B	(14.5)	(386)	(189)
19D	97	51	84
20	(1.81)	(717)	(4355)

Example	OT % inhibition @ 100 nM (IC_{50}, nM)*	V_{1a} % inhibition @ 100 nM (IC_{50}, nM)*	V_2 % inhibition @ 100 nM (IC_{50}, nM)*
21	(1.7)	(378)	(1163)
22	(1.74)	(225)	(1428)
24	(8.0)	(22.5)	(4.7)
25	(55.8)	(130.6)	(11.3)
26	17	-3	3
27	(18.1)	(45.6)	(148.9)
28	(29.51)	(66.56)	(58.82)
29	51	74	24
30	48	8	3
31	69	30	31
32	(185)	(> 3000)	(605)
33	101	68	11
43	(1.66)	(312)	(409)
47	(6.61)	(1004)	(722)
48	(6.7)	(484)	(700)
49	92	5	27
50	95	40	15
51	81	14	17
52	86	54	17
53	89	38	23
54	78	-4	7
55	67	4	30
56	68	2	27
57	76	15	11
58	24	5	18
59	(16.45)	(1886)	(2307)
60	(5.39)	(681)	(1203)
61	(4.5)	(316.4)	(744.6)
62	91	10	27
63	98	57	9
64	74	13	19
65	68	40	6
66	87	52	20
67	79	-4	4
68	64	9	29
69	71	8	22
70	75	19	11
71	25	4	13
72	74	8	26
73	85	46	21
74	45	12	14
75	66	27	14
76	65	58	17
77	65	44	28

Example	OT % inhibition @ 100 nM (IC_{50}, nM)*	V_{1a} % inhibition @ 100 nM (IC_{50}, nM)*	V_2 % inhibition @ 100 nM (IC_{50}, nM)*
78	62	-3	14
79	35	0	7
80	44	16	43
81	43	4	21
82	50	37	10
83	10	8	18
84	48	1	11
85	(3.02)	(788)	(3126)
86	(2.31)	(172)	(1698)
87	(4.63)	(349)	(2176)
88	98	44	30
89	97	50	13
90	100	63	19
91	97	90	17
92	99	78	20
93	90	29	36
94	94	28	26
95	97	68	13
96	54	10	24
97	(7.14)	(1092)	(2004)
98	(2.48)	(238)	(1026)
99	(2.04)	(311)	(1333)
100	98	27	26
101	100	75	7
102	95	45	18
103	98	43	11
104	96	85	20
105	97	74	18
106	88	22	34
107	87	15	19
108	96	52	8
109	49	9	14
110	(7.93)	(661)	(788)
111	(6.7)	(458.7)	(772.3)
112	89	8	32
113	97	45	9
114	76	11	22
115	**25**	**11**	**12**
116	84	42	22
117	70	-3	14
118	54	14	39
119	58	9	15
120	69	20	6
121	0	0	13

Example	OT % inhibition @ 100 nM (IC_{50}, nM)*	V_{1a} % inhibition @ 100 nM (IC_{50}, nM)*	V_2 % inhibition @ 100 nM (IC_{50}, nM)*
122	77	8	8
123	47	9	15
124	60	16	21
125	**36**	**10**	**8**
126	43	9	18
127	**29**	**16**	**3**
128	43	18	17
129	52	6	5
130	46	4	5
131	26	8	13
132	31	2	16
133	46	20	8
134	15	5	16
135	24	2	1
136	(7.19)	(538)	(597)
137	88	4	-4
138	95	47	29
139	76	9	12
140	87	24	29
141	-6	-3	8
142	83	46	-5
143	69	-3	7
144	53	-1	3
145	53	-4	-5
146	78	37	12
147	33	3	20
148	78	-9	1
149	75	17	20
150	75	42	18
151	47	17	6
152	63	23	10
153	60	50	11
154	54	39	9
155	56	0	15
156	30	2	12
157	38	5	23
158	50	16	19
159	50	44	16
160	20	6	24
161	53	8	4
162	71	18	20
163	82	43	13
164	54	23	16
165	64	24	25

Example	OT % inhibition @ 100 nM (IC_{50}, nM)*	V_{1a} % inhibition @ 100 nM (IC_{50}, nM)*	V_2 % inhibition @ 100 nM (IC_{50}, nM)*
166	27	29	3
167	60	50	20
168	52	8	10
169	36	9	5
170	47	21	27
171	40	14	14
172	47	43	11
173	21	0	17
174	59	8	7
175	98	28	17
176	88	27	18
177	98	42	18
178	93	79	15
179	93	73	23
180	98	26	14
181	100	23	12
182	70	14	35
183	97	26	18
184	83	0	9
185	95	37	27
186	97	53	8
187	100	81	31
188	96	89	10
189	99	83	22
190	99	40	9
191	100	41	17
192	91	31	28
193	96	41	16
194	96	23	0
195	(3.84)	(367)	(298)
196	(11.63)	(1243)	(855)
197	(5.39)	(524)	(497)
198	94	50	19
199	84	23	6
200	87	64	10
201	86	43	19
202	73	2	8
203	62	4	28
204	72	16	6
205	24	-6	18
206	(3.66)	(317)	(190)
207	(9.5)	(488)	(601.1)
208	81	20	12

Example	OT % inhibition @ 100 nM (IC_{50}, nM)*	V_{1a} % inhibition @ 100 nM (IC_{50}, nM)*	V_2 % inhibition @ 100 nM (IC_{50}, nM)*
209	81	64	10
210	82	39	17
211	87	45	23
212	95	35	43
213	70	12	33
214	64	8	11
215	26	5	22
216	82	10	0
217	98	21	34
218	98	45	23
219	(12.07)	(1807)	(1324)
220	(7.2)	(387)	(1816)
221	(11.1)	(818)	(832.7)
222	84	15	1
223	71	12	13
224	-3	1	7
225	87	35	-4
226	71	3	10
227	69	2	2
228	77	22	20
229	19	8	27
230	67	3	4
231	63	7	-5
232	81	13	4
233	86	31	23
234	82	26	22
235	64	9	17
236	46	6	5
237	79	39	-3
238	79	3	27
239	61	2	16
240	62	1	9
241	51	-4	-17
242	69	33	25
243	17	5	21
244	68	44	9
245	(16.91)	(933)	(423)
246	(17.8)	(373)	(508.2)
247	97	62	21
248	77	17	7
249	18	12	9
250	87	53	-10
251	87	6	24
252	72	8	21

Example	OT % inhibition @ 100 nM (IC_{50}, nM)*	V_{1a} % inhibition @ 100 nM (IC_{50}, nM)*	V_2 % inhibition @ 100 nM (IC_{50}, nM)*
253	71	16	-10
254	66	7	-4
255	80	53	27
256	33	7	40
257	85	10	16
258	(2.85)	(913)	(5679)
259	97	21	-3
260	102	55	20
261	52	13	18
262	76	8	4
263	(2.31)	(202)	(4124)
264	94	67	12
265	100	31	10
266	97	49	-17
267	93	12	24
268	90	6	34
269	88	-1	-19
270	95	40	25
271	(6.29)	(983)	(1915)
272	(2.61)	(301)	(1302)
273	(4.26)	(481.07)	(811.98)
274	103	90	32
275	89	9	21
276	74	4	-3
277	41	8	19
278	(7.87)	(303)	(1679)
279	100	39	17
280	95	77	6
281	93	58	-9
282	84	1	-17
283	91	40	29
284	87	0	12
285	93	38	32
286	86	8	27
287	88	0	26
288	95	24	32
289	45	6	7
290	78	47	-6
291	32	2	5
292	69	6	-7
293	53	2	3
294	54	-3	-2
295	79	6	22
296	88	31	24

Example	OT % inhibition @ 100 nM (IC_{50}, nM)*	V_{1a} % inhibition @ 100 nM (IC_{50}, nM)*	V_2 % inhibition @ 100 nM (IC_{50}, nM)*
297	73	-2	13
298	94	20	29
299	86	14	22
300	72	-2	19
301	82	1	9
302	64	-15	17
303	66	-4	14
304	74	-7	19
306	34	0	0
307	30	-7	8
308	7	-12	1
309	72	11	7
310	58	4	12
311	16	-5	7
312	16	7	3
313	32	2	2
314	19	6	7
315	10	7	-4
316	24	0	-2
317	32	10	15
318	32	5	17
319	22	9	13
320	34	4	21
321	62	5	23
322	66	12	24
323 F	33	2	5

* Binding in Chinese Hamster Ovary cell membranes expressing human vasopressin V_{1a} and V_2 subtype receptors, and human oxytocin receptors

The following Examples are presented to illustrate rather than limit the scope of this invention.

Example 1

10-[(2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid

Step A. 4-Bromo-3-methylbenzoic acid methyl ester

To a suspension of 4-bromo-3-methylbenzoic acid (10.0 g, 46.5 mmol) in methanol (125 mL) was added concentrated sulfuric acid (1 mL). The reaction was heated at reflux overnight with a homogeneous solution obtained after several minutes of heating. After cooling, the methanol was removed in vacuo and the residue was dissolved in dichloromethane and washed with saturated aqueous sodium bicarbonate. The organic phase was dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give 10.2 g of title compound as a brown solid, m.p. 41-43 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.39 (s, 3H), 3.85 (s, 3H), 7.64-7.72 (m, 2H), 7.88-7.89 (m, 1H).

MS [EI, m/z]: 228 $[M]^+$.

Anal. Calcd. for $C_9H_9BrO_2$: C 47.19, H 3.90. Found: C 47.22, H 3.80.

Step B. (2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carboxylic acid methyl ester

A mixture of 4-bromo-3-methylbenzoic acid methyl ester of Step A (2.0 g, 8.7 mmol), 2-trifluoromethyl-phenyl boronic acid (1.65 g, 8.7 mmol) and sodium carbonate (4.1 g, 38.7 mmol) in toluene:ethanol:water (50 mL: 25 mL: 25 mL) was purged with nitrogen for 1 hour. After addition of the tetrakis(triphenylphosphine) palladium(0) catalyst (0.50 g, 0.43 mmol) the reaction was heated at 100 °C overnight. The cooled reaction mixture was filtered through Celite and the cake washed with ethyl acetate. The organic layer was washed with water, dried over anhydrous. sodium sulfate, filtered and concentrated in vacuo to give a brown oil. Purification by flash chromatography with a solvent gradient of 25% to 50% dichloromethane in hexane provided 2.0 g of the title compound as a colorless oil.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.03 (s, 3H), 3.88 (s, 3H), 7.26 (d, 1H), 7.34 (d, 1H), 7.66 (t, 1H), 7.75 (t, 1H), 7.81-7.83 (m, 1H), 7.86-7.88 (m, 1H), 7.90-7.91 (m, 1H).

MS [(+)ESI, m/z]: 312 $[M+NH_4]^+$.

Anal. Calcd. for $C_{16}H_{13}F_3O_2$: C 65.31, H 4.45. Found: C 64.92, H 4.54.

Step C. (2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carboxylic acid

To a solution of (2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carboxylic acid methyl ester of Step B (1.9 g, 6.5 mmol) in tetrahydrofuran (30 mL) was added 1 N sodium hydroxide (13 mL, 13 mmol). The reaction mixture was heated at reflux overnight, then cooled and acidified with 2 N hydrochloric acid. The aqueous layer was extracted with ethyl acetate and the combined extracts were dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give 1.65 g of the title compound as a white solid, m.p. 171-174 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.02 (s, 3H), 7.23 (d, 1H), 7.34 (d, 1H), 7.65 (t, 1H), 7.75 (t, 1H), 7.79-7.81 (m, 1H), 7.86-7.89 (m, 2H), 13.00 (br s, 1H).

MS [(-)ESI, m/z]: 279 $[M-H]^-$.

Anal. Calcd. for $C_{15}H_{11}F_3O_2$: C 64.29, H 3.96. Found: C 64.26, H 3.80.

Step D. (10,11-Dihydro-5H-pyrrolo [2,1-c][1,4]benzodiazepin-10-yl)-[(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]methanone

A suspension of (2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carboxylic acid of Step C (0.50 g, 1.78 mmol) in thionyl chloride (3 mL) was heated at reflux for 90 minutes. After cooling, the thionyl chloride was removed in vacuo and the residue dissolved in toluene. The solution was concentrated in vacuo to yield the crude acid chloride as a brown oil. The acid chloride was dissolved in dichloromethane (5 mL) and slowly added to a solution of 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine (0.49 g, 2.66 mmol) and N,N-diisopropylethyl amine (0.68 mL, 3.90 mmol) in dichloromethane (15 mL). After stirring for 2 hours, the reaction was quenched with water. The organic layer was sequentially washed with 1 N hydrochloric acid, 1 N sodium hydroxide and brine, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a yellow foam. Purification by flash chromatography on silica gel using a solvent gradient of 15 to 25% ethyl acetate in hexane gave a white foam which was crystallized upon sonication in ethanol/hexane to provide the title compound (0.55 g) as a white solid, m.p. 127-130 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.86 (s, 3H), 4.80-5.40 (br, 4H), 5.93-5.98 (m, 2H), 6.85 (t, 1H), 6.91-6.96 (m, 2H), 7.03-7.05 (m, 1H), 7.10-7.14 (m, 1H), 7.19-7.24 (m, 2H), 7.29 (s, 1H), 7.47-7.49 (m, 1H), 7.61 (t, 1H), 7.70 (t, 1H), 7.81 (d, 1H).

MS [EI, m/z]: 446 $[M]^+$.

Anal. Calcd. for $C_{27}H_{21}F_3N_2O$: C 72.64, H 4.74, N 6.27. Found: C 72.48, H 4.57, N 6.16.

Step E. 2,2,2-Trichloro-1-(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10.11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-3-yl)ethanone

To a solution of (10,11-dihydro-5H-pyrrolo [2,1-c][1,4]benzodiazepin-10-yl]-[(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]methanone of Step D (1.87 g, 4.19 mmol) in dichloromethane (20 mL) was added N,N-diisopropylethyl amine (1.46 mL, 8.38 mmol) followed by the slow addition of trichloroacetyl chloride (1.45 mL, 13.0 mmol). The reaction mixture was stirred overnight at room temperature, and then quenched with water. The organic phase was washed with 0.1 N hydrochloric acid followed by water, then dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a green oil. Purification by flash chromatography on silica gel using a solvent system of 20% ethyl acetate in hexane provided 2.2 g of title product as a pale, yellow foam.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.84 (s, 3H), 5.25 (br, 2H), 5.97 (br, 2H), 6.37 (d, 1H), 6.89-6.92 (m, 2H), 7.02-7.04 (m, 1H), 7.06-7.10 (m, 1H), 7.15-7.22 (m, 2H), 7.28 (s, 1H), 7.41-7.46 (m, 2H), 7.58 (t, 1H), 7.67 (t, 1H), 7.79 (d, 1H).

MS [(+)APCI, m/z]: 591 $[M+H]^+$.

Anal. Calcd. for $C_{29}H_{20}Cl_3F_3N_2O_2$ + 0.20 $C_4H_8O_2$ + 0.80 H_2O: C 57.37, H 3.75, N 4.49. Found: C 57.06, H 3.39, N 4.50.

Step F. 10-[(2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid

To a solution of 2,2,2-trichloro-1-(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-3-yl)ethanone of Step E (2.3 g, 3.9 mmol) in acetone (20 mL) was added 2.5 N sodium hydroxide (3.1 mL, 7.8 mmol). After stirring overnight, the reaction mixture was acidified with 2 N hydrochloric acid (4.3 mL, 8.6 mmol) and then concentrated in vacuo. The residue was partitioned between ethyl acetate and water. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a brown solid. Trituration with diethyl ether/hexane provided the title compound (1.32 g) as a white solid, m.p. 233-235 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.84 (s, 3H), 5.17 (br, 2H), 5.94 (br, 2H), 6.10-6.11 (m, 1H), 6.76 (d, 1H), 6.85-6.91 (m, 2H), 7.00-7.06 (m, 2H), 7.12-7.16 (m, 1H), 7.21 (d, 1H), 7.25 (s, 1H), 7.32-7.34 (m, 1H), 7.59 (t, 1H), 7.68 (t, 1H), 7.79 (d, 1H), 12.33 (br, 1H).

MS [(+)ESI, m/z]: 491 $[M+H]^+$.

Anal. Calcd. for $C_{28}H_{21}F_3N_2O_3$: C 68.57, H 4.32, N 5.71.

Found: C 68.39, H 4.25, N 5.64.

Example 2

(4-Methyl-piperazin-1-yl)-[10-(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-3-yl-methanone

A suspension of 10-[(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid of Example 1, Step F (1.65 g, 3.36 mmol) in dichloromethane (15 mL) containing a few drops of N,N-dimethylformamide was treated dropwise under nitrogen with oxalyl chloride (0.38 mL, 4.36 mmol). After the gas evolution subsided, the reaction mixture was refluxed for an additional 15 min. The cooled solution was evaporated to dryness to give the crude acid chloride as a brown solid. The acid chloride was then dissolved in dichloromethane (10 mL) and slowly added to a solution of 1-methylpiperazine (1.5 mL, 13.5 mmol) and N,N-diisopropylethyl amine (3.5 mL, 20.1 mmol) in dichloromethane (25 mL). After stirring overnight, the reaction was quenched with water. The organic layer was sequentially washed with 1 N hydrochloric acid, 1 N sodium hydroxide and brine, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a brown oil. Purification by flash chromatography on silica gel using a solvent system of 10% methanol in ethyl acetate gave a pale yellow foam which was crystallized from diethyl ether to provide the desired title compound (1.17 g) as a white solid.

^1H NMR (DMSO-d_6, 400 MHz): δ 1.83 (s, 3H), 2.20 (s, 3H), 2.31-2.33 (m, 4H), 3.61-3.63 (m, 4H), 5.15 (br, 2H), 5.40 (s, 2H), 6.06 (d, 1H), 6.23 (d, 1H), 6.85-6.90 (m, 2H), 6.99-7.06 (m, 2H), 7.12-7.16 (m, 1H), 7.20 (d, 1H), 7.25 (s, 1H), 7.37-7.39 (m, 1H), 7.58 (t, 1H), 7.67 (t, 1H), 7.79 (d, 1H).

MS [(+)ESI, m/z]: 573 $[M+H]^+$.

Anal. Calcd. for $C_{33}H_{31}F_3N_4O_2$: C 69.22, H 5.46, N 9.78.

Found: C 68.79, H 5.45, N 9.72.

Example 3

10-[(2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid bis-(3-dimethylamino-propyl)-amide

A suspension of 10-[(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid of Example 1, Step F (0.50 g, 1.02 mmol) in dichloromethane (5 mL) containing a few drops of N,N-dimethylformamide was treated dropwise under nitrogen with oxalyl chloride (0.12 mL, 1.38 mmol). After gas evolution subsided, the reaction mixture was refluxed for an additional 15 minutes. The cooled solution was evaporated to dryness to give the crude acid chloride as a brown solid. The acid chloride was then dissolved in dichloromethane (5 mL) and slowly added to a solution of bis-(3-dimethylamino-propyl)-amine (0.90 mL, 4.04 mmol) and N,N-diisopropylethyl amine (1.1 mL, 6.31 mmol) in dichloromethane (5 mL). After stirring for 2 hours, the reaction was quenched with water. The organic layer was sequentially washed with 1 N hydrochloric acid, 1 N sodium hydroxide and brine, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a brown oil. Purification was achieved by preparative HPLC on a Primesphere 5 C18 column (0.21 x 15 cm) using a solvent gradient from 60:40:0.1 to 80:20:0.1 acetonitrile-water-trifluoroacetic acid. After removal of the acetonitrile in vacuo, the aqueous solution was basified with 2.5 N sodium hydroxide then extracted with dichloromethane. The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give the title compound (0.24 g) as a white foam, m.p. 55-64°C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.68 (br, 4H), 1.83 (s, 3H), 2.00-2.23 (br, 16H), 3.43 (t, 4H), 5.10 (br, 2H), 5.34 (s, 2H), 6.04 (d, 1H), 6.21 (d, 1H), 6.87-6.90 (m, 2H), 6.99-7.04 (m, 2H), 7.13 (t, 1H), 7.21 (d, 1H), 7.24 (s, 1H), 7.31-7.33 (m, 1H), 7.58 (t, 1H), 7.67 (t, 1H), 7.79 (d, 1H).

MS [(+)ESI, m/z]: 660 $[M+H]^+$.

Anal. Calcd. for $C_{38}H_{44}F_3N_5O_2$: C 69.18, H 6.72, N 10.61. Found: C 68.26, H 6.68, N 10.43.

Example 4

[4-(3-Dimethylaminopropyl)-piperazin-1-yl]-[10-(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-[10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl]-methanone

10-[(2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid of Example 1, Step F (0.50 g, 1.02 mmol), 1-[3-(dimethylamino)propyl] piperazine (0.21 mL, 1.23 mmol) and 1-hydroxy-benzotriazole monohydrate (0.15 g, 1.11 mmol) were dissolved in N,N-dimethyl-formamide (4 mL). 1-[3-(dimethylamino)propyl]-3-ethyl carbodiimide hydrochloride (0.22 g, 1.15 mmol) was then added followed by N,N-diisopropylethyl amine (0.27 mL, 1.55 mmol). The reaction mixture was stirred overnight, diluted with ethyl acetate and washed with water and saturated aqueous sodium bicarbonate. The organic phase was dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a yellow oil. Purification by flash chromatography on silica gel using a solvent system of 10% methanol in chloroform provided the title compound (0.19 g) as a white foam, m.p. 85-95°C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.52-1.60 (m, 2H), 1.83 (s, 3H), 2.13 (s, 6H), 2.25 (t, 2H), 2.31 (t, 2H), 2.37 (br, 4H), 3.61 (br, 4H), 5.15 (br, 2H), 5.40 (s, 2H), 6.05 (d, 1H), 6.22 (d, 1H), 6.84-6.90 (m, 2H), 6.98-7.06 (m, 2H), 7.14 (t, 1H), 7.21 (d, 1H), 7.25 (s, 1H), 7.37-7.39 (m, 1H), 7.58 (t, 1H), 7.68 (t, 1H), 7.79 (d, 1H).

MS [(+)ESI, m/z]: 644 $[M+H]^+$.

Anal. Calcd. for $C_{37}H_{40}F_3N_5O_2$ + 0.40 H_2O: C 68.26, H 6.32, N 10.76.

Found: C 67.94, H 6.37, N 10.46.

Example 5

[3-Methyl-4-(3-methyl-phenyl)-piperazin-1-yl]-[10-(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl-methanone

10-[(2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid of Example 1, Step F (0.50 g, 1.02 mmol), 2-methyl-1-(3-methylphenyl)piperazine (0.24 mL, 1.26 mmol) and 1-hydroxy-

benzotriazole monohydrate (0.15 g, 1.11 mmol) were dissolved in N,N-dimethylformamide (5 mL). 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (0.22 g, 1.15 mmol) was then added followed by N,N-diisopropylethyl amine (0.27 mL, 1.55 mmol). The reaction mixture was stirred overnight, diluted with ethyl acetate and washed with water and saturated aqueous bicarbonate. The organic phase was then dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a brown oil. Purification by flash chromatography on silica gel using a solvent system of 40% ethyl acetate in hexane provided a white foam which was redissolved in dichloromethane and evaporated to dryness in vacuo prior to use in the next step.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 0.91 (d, 3H), 1.83 (s, 3H), 2.24 (s, 3H), 3.00-3.05 (m, 1H), 3.28-3.32 (m, 2H), 3.46-3.49 (m, 1H), 3.99-4.07 (m, 2H), 4.22-4.25 (m, 1H), 5.15 (br, 2H), 5.40-5.49 (m, 2H), 6.09 (d, 1H), 6.31 (d, 1H), 6.59 (d, 1H), 6.70-6.73 (m, 2H), 6.85-6.90 (m, 2H), 6.99-7.15 (m, 4H), 7.20 (d, 1H), 7.26 (s, 1H), 7.36 (d, 1H), 7.58 (t, 1H), 7.67 (t, 1H), 7.79 (d, 1H).

MS [(+)ESI, m/z]: 663 $[M+H]^+$.

Anal. Calcd. for $C_{40}H_{37}F_3N_4O_2$ + 0.13 CH_2Cl_2 + 0.17 $C_4H_8O_2$: C 71.17, H 5.65, N 8.13. Found: C 70.85, H 5.50, N 8.01.

Example 6

4-[[10,11-Dihydro-10-[[2-methyl-2'-trifluoromethyl[1,1'-biphenyl]-4-yl]carbonyl]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl]carbonyl]-1-piperazine-carboxylic acid, tert-butyl ester

10-[(2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid of Example 1, Step F (1.0 g, 2.04 mmol), 1-(tert-butoxycarbonyl)piperazine (0.46 g, 2.47 mmol) and 1-hydroxybenzotriazole monohydrate (0.30 g, 2.22 mmol) were dissolved in N,N-dimethylformamide (8 mL). 1-[3-(dimethylamino)propyl]-3-ethyl carbodiimide hydrochloride (0.43 g, 2.24 mmol) was then added followed by N,N-diisopropylethyl amine (0.55 mL, 3.09 mmol). The reaction mixture was stirred overnight, diluted with ethyl acetate and washed with water and saturated aqueous sodium bicarbonate. The organic phase was then dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a brown oil. Purification by flash chromatography using a solvent gradient from 30% to 50% ethyl

acetate in hexane provided the desired title compound as a white foam, which was redissolved in dichloromethane and evaporated to dryness in vacuo prior to use in the next step.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.41 (s, 9H), 1.83 (s, 3H), 3.38 (br, 4H), 3.59-3.61 (m, 4H), 5.15 (br, 2H), 5.41 (s, 2H), 6.07 (d, 1H), 6.28 (d, 1H), 6.85-6.90 (m, 2H), 6.99-7.06 (m, 2H), 7.12-7.16 (m, 1H), 7.21 (d, 1H), 7.25 (s, 1H), 7.40-7.42 (m, 1H), 7.58 (t, 1H), 7.67 (t, 1H), 7.79 (d, 1H).

MS [(+)APCI, m/z]: 659 $[M+H]^+$.

Anal. Calcd. for $C_{37}H_{37}F_3N_4O_4$ + 0.09 CH_2Cl_2 + 0.18 $C_4H_8O_2$: C 66.56, H 5.71, N 8.21. Found; C 66.27, H 5.40, N 8.00.

Example 7

10,11-Dihydro-10-[[2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl]-3-(1-piperazinylcarbonyl)-5H-pyrrolo[2,1-c][1,4]benzodiazepine hydrochloride salt

The 4-[[10,11-dihydro-10-[[2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl]carbonyl]-1-piperazine-carboxylic acid, tert-butyl ester of Example 6 (0.85 g, 1.29 mmol) was added in one portion to stirred ethyl acetate (10 mL) saturated with hydrogen chloride gas at 0 °C. A precipitate formed after several minutes. The reaction mixture was stirred for 90 minutes under anhydrous conditions. The reaction was then warmed to room temperature and diluted with diethyl ether. The precipitated product was collected by filtration and dried under high vacuum to provide the desired title compound hydrochloride salt (0.65 g) as an off-white foam.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.84 (s, 3H), 3.16 (br, 4H), 3.83-3.85 (m, 4H), 5.15 (br, 2H), 5.43 (s, 2H), 6.09 (d, 1H), 6.38 (d, 1H), 6.87-6.91 (m, 2H), 6.99-7.01 (m, 1H), 7.06 (t, 1H), 7.13-7.17 (m, 1H), 7.21 (d, 1H), 7.26 (s, 1H), 7.44-7.46 (m, 1H), 7.59 (t, 1H), 7.68 (t, 1H), 7.79 (d, 1H), 9.28 (br, 2H).

MS [(+)APCI, m/z]: 559 $[M+H]^+$.

Anal. Calcd. for $C_{32}H_{29}F_3N_4O_2$ + 1.0 HCl + 1.00 H_2O + 0.06 $C_4H_{10}O$: C 62.70, H 5.32, N 9.07. Found: C 62.42, H 5.22, N 8.94.

Example 8

N-[(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)carbonyl]guanidine

10-[(2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid of Example 1, Step F (0.50 g, 1.02 mmol) and 1,1'-carbonyldiimidazole (0.17 g, 1.05 mmol) were dissolved in anhydrous N,N-dimethylformamide (5 mL). After stirring for 30 minutes, guanidine carbonate (0.19 g, 1.05 mmol) was added, and the reaction was heated to 100 °C for 4 hours. After cooling, the reaction mixture was diluted with water and extracted with ethyl acetate. The organic layers were combined and dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give an orange oil. Purification was achieved by preparative HPLC on a Primesphere 5 C18 (0.2 x 15 cm) column using a solvent gradient from 55:45:0.1 to 90:10:0.1 acetonitrile-water-trifluoroacetic acid. After removal of the acetonitrile in vacuo, the aqueous solution was neutralized with saturated aqueous sodium bicarbonate, and then extracted with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give 0.25 g of the title compound as a white solid.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.85 (s, 3H), 5.15 (br, 2H), 6.00 (d, 1H), 6.20 (br, 2H), 6.65 (d, 1H), 6.80 (d, 1H), 6.97 (d, 1H), 6.96-7.01 (m, 2H), 7.11 (t, 1H), 7.22-7.25 (m, 2H), 7.36-7.38 (m, 1H), 7.60 (t, 1H), 7.69 (t, 1H), 7.80 (d, 1H).

MS [(+)APCI, m/z]: 532 $[M+H]^+$.

Anal. Calcd. for $C_{29}H_{24}F_3N_5O_2$ + 0.15 $C_4H_8O_2$: C 65.26, H 4.66, N 12.86.

Found: C 64.53, H 4.45, N 12.77.

Example 9

10-[(2'-Methoxy-2-methyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4]benzodiazepine-3-carboxylic acid

Step A. (2-Methyl-2'-methoxy-[1,1'-biphenyl]-4-yl)carboxylic acid methyl ester

A mixture of 3-methyl-4-bromobenzoic acid methyl ester (2.0 g, 8.7 mmol), 2-methoxyphenyl boronic acid (1.32 g, 8.7 mmol) and sodium carbonate (4.1 g, 38.7 mmol) in toluene:ethanol:water (50 mL:25 mL: 25 mL) was purged with nitrogen for 1 hour.

After addition of the tetrakis(triphenylphosphine) palladium(0) catalyst (0.50 g, 0.43 mmol), the reaction mixture was heated at 100 °C overnight. After cooling, the reaction was filtered through Celite and the cake washed with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a brown oil. Purification by flash chromatography on silica gel with a solvent gradient from 20% to 50% dichloromethane in hexane gave 2.0 g of product as a colorless oil.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.09 (s, 3H), 3.70 (s, 3H), 3.85 (s, 3H), 7.00-7.04 (m, 1H), 7.08-7.11 (m, 2H), 7.23 (d, 1H), 7.37-7.41 (m, 1H), 7.77-7.79 (m, 1H), 7.83-7.84 (m, 1H).

MS [(+)APCI, m/z]: 257 $[M+H]^+$.

Anal. Calcd. for $C_{16}H_{16}O_3$: C 74.98, H 6.29. Found: C 74.06, H 6.17.

Step B. (2-Methyl-2'-methoxy-[1,1'-biphenyl]-4-yl)carboxylic acid

The (2-methyl-2'-methoxy-[1,1'-biphenyl]-4yl)carboxylic acid methyl ester of Step A (1.9 g, 7.4 mmol) was dissolved in tetrahydrofuran (30 mL) and 1 N sodium hydroxide (15 mL, 15 mmol) was added. The reaction mixture was heated at reflux overnight, then cooled and acidified with 2 N hydrochloric acid. The aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give 1.6 g of product as a white solid, m.p. 160-162°C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.09 (s, 3H), 3.70 (s, 3H), 7.00-7.03 (m, 1H), 7.08-7.10 (m, 2H), 7.20 (d, 1H), 7.36-7.40 (m, 1H), 7.75-7.78 (m, 1H), 7.82 (s, 1H), 12.85 (br, 1H).

MS [(-) APCI, m/z]: 241 $[M-H]^-$.

Anal. Calcd. for $C_{15}H_{14}O_3$: C 74.36, H 5.82. Found: C 73.93, H 5.71.

Step C. (10,11-Dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-10-yl)- (2'-methoxy-2-methyl-[1,1'-biphenyl]-4-yl)-methanone

The (2-methyl-2'-methoxy-[1,1'-biphenyl]-4-yl)carboxylic acid of Step B (0.50 g, 2.06 mmol) was suspended in thionyl chloride (3 mL) and the mixture heated at reflux for 30 minutes. After cooling, the thionyl chloride was removed in vacuo. The residue was dissolved in toluene and concentrated in vacuo to give the crude acid chloride as a brown oil. The acid chloride was then dissolved in dichloromethane (5 mL) and slowly

added to a solution of 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine (0.57 g, 3.10 mmol) and N,N-diisopropylethyl amine (0.79 mL, 4.53 mmol) in dichloromethane (15 mL). After stirring for 1 hour, the reaction was quenched with water. The organic layer was washed with 1 N hydrochloric acid, 1 N sodium hydroxide and brine, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a yellow foam. Purification by flash chromatography using a solvent gradient of 5 to 15% ethyl acetate in hexane yielded a white foam which crystallized upon sonication in ethanol/hexane to give 0.42 g of the desired title product as a white solid, m.p. 133-135 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.93 (s, 3H), 3.65 (s, 3H), 4.80-5.40 (br, 4H), 5.92-5.96 (m, 2H), 6.81-6.82 (m, 1H), 6.89-6.91 (m, 1H), 6.95-7.05 (m, 5H), 7.16-7.25 (m, 3H), 7.31-7.35 (m, 1H), 7.47-7.49 (m, 1H).

MS [(+)ESI, m/z]: 409 $[M+H]^+$.

Anal. Calcd. for $C_{27}H_{24}N_2O_2$: C 79.39, H 5.92, N 6.86. Found: C 79.16, H 5.87, N 6.90.

Step D. 2,2,2-Trichloro-1-{10-[(2'-methoxy-2-methyl-[1,1'-biphenyl]-4-yl)carbonyl]- 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-3-yl} ethanone

To a solution of (10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl)-(2'-methoxy-2-methyl-[1,1'-biphenyl]-4-yl)-methanone of Step C (1.5 g, 3.67 mmol) in dichloromethane (20 mL) was added N,N-diisopropylethyl amine (1.28 mL, 7.35 mmol) followed by slow addition of trichloroacetyl chloride (1.23 mL, 11.0 mmol). The reaction mixture was stirred overnight at room temperature then quenched with water. The organic phase was washed with 0.1 N hydrochloric acid followed by water, then dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a green oil. Purification by flash chromatography on silica gel using a solvent system of 20% ethyl acetate in hexane provided 2.1 g of title compound. The material was redissolved in dichloromethane and evaporated to dryness to provide a yellow foam, which was used in the next step.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.94 (s, 3H), 3.65 (s, 3H), 5.25 (br, 2H), 5.97 (br, 2H), 6.36-6.37 (m, 1H), 6.90-6.92 (m, 1H), 6.96-7.06 (m, 5H), 7.15-7.23 (m, 2H), 7.26 (s, 1H), 7.32-7.36 (m, 1H), 7.44-7.47 (m, 2H).

MS [(+)APCI, m/z]: 553 $[M+H]^+$.

Anal. Calcd. for $C_{29}H_{23}Cl_3N_2O_3$ + 0.13 $C_4H_8O_2$ + 0.13 CH_2Cl_2:C 61.79, H 4.25, N 4.86. Found: C 60.43, H 4.50, N 4.80.

Step E. 10-[(2'-Methoxy-2-methyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H- pyrrolo [2,1-c][1,4]benzodiazepine-3-carboxylic acid

To a solution of 2,2,2-trichloro-1-{10-[(2'-methoxy-2-methyl-[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-3-yl} ethanone of Step D (2.0 g, 3.6 mmol) in acetone (20 mL) was added 2.5 N sodium hydroxide (2.9 mL, 7.25 mmol). After stirring overnight, the reaction mixture was acidified with 2 N hydrochloric acid (4.0 mL, 8.0 mmol) then concentrated in vacuo. The residue was partitioned between ethyl acetate and water. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a brown solid. Trituration with diethyl ether-hexane provided 1.4 g of the desired product as a white solid, m.p.174-184 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.93 (s, 3H), 3.65 (s, 3H), 5.17 (br, 2H), 5.94 (br, 2H), 6.09-6.10 (m, 1H), 6.77 (d, 1H), 6.89-7.06 (m, 6H), 7.10-7.19 (m, 2H), 7.23 (s, 1H), 7.31-7.38 (m, 2H), 12.31 (br, 1H).

MS [(-)APCI, m/z]: 451 $[M-H]^-$.

Anal. Calcd. for $C_{28}H_{24}N_2O_4$ + 0.10 $C_4H_{10}O$: C 74.17, H 5.48, N 6.09.

Found: C 73.63, H 5.68, N 5.94.

Example 10

10-[(3-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepine-3-carboxylic acid

Step A. 4-Iodo-2-methoxybenzoic acid methyl ester

4-Amino-2-methoxybenzoic acid methyl ester (3.0 g, 16.6 mmol) was suspended in water (40 mL) and concentrated sulfuric acid (10 mL) was added. The suspension was cooled in an ice/salt water bath, and an aqueous solution (10 mL) of sodium nitrite (1.26 g, 18.3 mmol) was added dropwise so that the temperature remained close to 0 °C. After the addition, a homogeneous, yellow-green solution was obtained. An aqueous solution (60 mL) of potassium iodide (3.02 g, 18.2 mmol) and iodine (2.31 g, 9.1 mmol) was then added dropwise, and the reaction stirred for an additional 1 hour. The reaction mixture was then extracted with ethyl acetate, the organic extracts were combined and washed with 1 N sodium thiosulfate, 1 N sodium hydroxide and brine. After drying over

anhydrous sodium sulfate the solution was filtered and concentrated in vacuo to give 2.7 g of the title product as an orange oil which was used in the next step.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.76 (s, 3H), 3.82 (s, 3H), 7.39 (s, 2H), 7.48 (s, 1H).

MS [EI, m/z]: 292 $[M]^+$.

Step B. 4-Iodo-2-methoxybenzoic acid

The 4-iodo-2-methoxybenzoic acid methyl ester of Step A (2.7 g, 9.24 mmol) was dissolved in tetrahydrofuran (40 mL) and 1 N sodium hydroxide (20 mL, 20 mmol) was added. The reaction mixture was heated at reflux for 3 hours, then cooled and concentrated in vacuo to give an orange oil that was partitioned between ethyl acetate and 2 N hydrochloric acid. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give 2.5 g of title product as a yellow-orange solid, m.p. 144-146 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.81 (s, 3H), 7.37 (s, 2H), 7.44 (s, 1H), 12.72 (br,1H).

MS [EI, m/z]: 278 $[M]^+$.

Anal. Calcd. for $C_8H_7IO_3$ + 0.10 $C_4H_8O_2$: C 35.17, H 2.74. Found: C 35.37, H 2.49.

Step C. 10-(4-Iodo-2-methoxybenzoyl)-10,11-dihydro-5H-pyrrolo [2,1-c][1,4]-benzodiazepine

A suspension of 4-iodo-2-methoxybenzoic acid of Step B (2.5 g, 9.0 mmol) in thionyl chloride (10 mL) was heated at reflux for 1 hour. After cooling, the thionyl chloride was removed in vacuo. The residue was dissolved in toluene and concentrated in vacuo to give the crude acid chloride as a brown solid. The acid chloride was then dissolved in dichloromethane (10 mL) and slowly added to a solution of 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine (1.75 g, 9.5 mmol) and N,N-diisopropylethyl amine (3.4 mL, 19.5 mmol) in dichloromethane (20 mL). After stirring for 2 hours, the reaction was quenched with water. The organic layer was washed with 1 N hydrochloric acid, 1 N sodium hydroxide and brine, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a yellow foam. Purification by flash chromatography on silica gel using a solvent gradient of 15 to 25% ethyl acetate in hexane provided 3.6 g of title product as a white foam, which was redissolved in dichloromethane and evaporated to dryness prior to use in the next step.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.55 (br, 3H), 4.80-5.32 (br, 4H), 5.88-5.90 (m, 1H), 5.94 (s, 1H), 6.79 (s, 1H), 6.94 (s, 1H), 7.03 (t, 1H), 7.09-7.13 (m, 3H), 7.20-7.22 (m, 1H), 7.36-7.38 (m, 1H).

MS [(+)ESI, m/z]: 445 $[M+H]^+$.

Anal. Calcd. for $C_{20}H_{17}IN_2O_2$ + 0.10 $C_4H_8O_2$ + 0.13 CH_2Cl_2: C 53.13, H 3.92, N 6.04. Found: C 53.03, H 3.65, N 6.03.

Step D. (10,11-Dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-10-yl)-[3-methoxy-2'-methyl-[1,1'-biphenyl]-4-yl]-methanone

A mixture of 10-(4-iodo-2-methoxybenzoyl)-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine of Step C (1.8 g, 4.1 mmol), 2-methylphenyl boronic acid (0.55 g, 4.1 mmol) and sodium carbonate (1.9 g, 17.9 mmol) in toluene:ethanol: water (20 mL:10 mL:10 mL) was purged with nitrogen for 1 hour. After addition of the tetrakis(triphenyl-phosphine) palladium(0) catalyst (0.24 g, 0.21 mmol), the reaction mixture was heated at 100 °C overnight. After cooling, the reaction was filtered through Celite and the cake washed with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a brown oil. Purification by flash chromatography on silica gel using a solvent system of 20% ethyl acetate in hexane provided 1.5 g of title product as a white foam, which was redissolved in dichloromethane and evaporated to dryness in vacuo prior to use in the next step.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.08 (s, 3H), 3.54 (s, 3H), 4.80-5.30 (br, 4H), 5.89-5.91 (m, 1H), 5.97 (s, 1H), 6.66 (s, 1H), 6.77-6.80 (m, 2H), 6.93-7.01 (m, 2H), 7.09-7.10 (m, 2H), 7.19-7.24 (m, 3H), 7.36-7.38 (m, 2H).

MS [(+)ESI, m/z]: 409 $[M+H]^+$.

Anal. Calcd. for $C_{27}H_{24}N_2O_2$ + 0.10 CH_2Cl_2: C 78.05, H 5.84, N 6.72. Found: C 78.12, H 5.13, N 6.69.

Step E. 2,2,2-Trichloro-1-{10-[(3-methoxy-2'-methyl-[1,1'-biphenyl]-4- yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3- yl}ethanone

To a solution of (10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-10-yl)-[3-methoxy-2'-methyl-[1,1'-biphenyl]-4-yl]-methanone of Step D (1.36 g, 3.33 mmol) in dichloromethane (15 mL) was added N,N-diisopropylethyl amine (1.2 mL, 6.89 mmol) followed by slow addition of trichloroacetyl chloride (1.1 mL, 9.85 mmol). The reaction

mixture was stirred overnight at room temperature then was quenched with water. The organic phase was washed with 0.1 N hyrochloric acid followed by water, then dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a green oil. Purification by flash chromatography on silica gel using a solvent system of 20% ethyl acetate in hexane gave 1.7 g of title product as a yellow foam.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.09 (s, 3H), 3.50 (s, 3H), 5.30 (br, 2H), 5.87 (br, 2H), 6.37-6.38 (m, 1H), 6.64 (s, 1H), 6.82-6.83 (m, 1H), 6.90-6.92 (m, 1H), 6.97-6.99 (m, 1H), 7.10-7.12 (m, 2H), 7.20-7.25 (m, 4H), 7.35-7.37 (m, 1H), 7.44-7.46 (m, 1H).

MS [(+)APCI, m/z]: 553 $[M+H]^+$.

Anal. Calcd. for $C_{28}H_{23}Cl_3N_2O_3$+ 0.20 $C_4H_8O_2$ + 0.40 H_2O: C 61.85, H 4.42, N 4.84.
Found: C 61.50, H 4.07, N 4.72.

Step F. 10-[(3-Methoxy-2'-methyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid

To a solution of 2,2,2-trichloro-1-{10-[(3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3- yl}ethanone of Step E (1.6 g, 2.9 mmol) in acetone (20 mL) was added 2.5 N sodium hydroxide (2.3 mL, 5.8 mmol). After stirring overnight, the reaction was acidified with 2 N hydrochloric acid (3.2 mL, 6.4 mmol) then concentrated in vacuo. The residue was partitioned between ethyl acetate and water. The layers were separated, and the organic layer was dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a brown solid. Trituration with diethyl ether/hexane provided 1.2 g of desired product as an off-white solid, m.p. 201-204 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.09 (s, 3H), 3.48 (s, 3H), 5.20 (br, 2H), 5.85 (br, 2H), 6.12 (s, 1H), 6.62 (s, 1H), 6.73 (d, 1H), 6.79-6.87 (m, 2H), 6.91-6.95 (m, 1H), 6.99-7.03 (m, 1H), 7.06-7.12 (m, 1H), 7.18-7.25 (m, 4H), 7.39 (br, 1H), 12.31 (br, 1H).

MS [(+) ESI, m/z]: 453 $[M+Na]^+$.

Anal. Calcd. for $C_{28}H_{24}N_2O_4$+ 0.10 $C_4H_{10}O$ + 0.15 $C_4H_8O_2$: C 73.61, H 5.58, N 5.92.
Found: C 73.23, H 5.49, N 6.06.

Example 11

N-Methyl-N-[3-(dimethylamino)propyl]-10-[(3-methoxy-2'-methyl[1,1'-biphenyl]- 4-yl)carbonyl]- 10,11-dihydro-5H-pyrrolo[2,1- c][1,4]benzodiazepine-3-carboxamide

To a solution of 10-[(3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid of Example 10, Step F (0.40 g, 0.88 mmol), 3-(dimethylaminopropyl)-1-methyl amine (0.16 mL, 1.09 mmol) and 1-hydroxybenzotriazole (0.135 g, 0.96 mmol) in N,N-dimethylformamide (4 mL) was added 1-[3-(dimethylamino)propyl]-3-ethyl carbodiimide hydrochloride (0.19 g, 1.09 mmol) followed by N,N-diisopropylethyl amine (0.24 mL, 1.35 mmol). The reaction mixture was stirred overnight, then diluted with ethyl acetate and washed with water and saturated aqueous sodium bicarbonate. The organic phase was then dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a yellow foam. Purification by flash chromatography on silica gel using a solvent system of 5% methanol in dichloromethane afforded 0.36 g of title compound as a white foam.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.67-1.73 (m, 2H), 2.08-2.25 (m, 10H), 3.03 (s, 3H), 3.45-3.50 (m, 6H), 4.60-5.40 (br m, 4H), 6.05-6.06 (m, 1H), 6.25-6.26 (m, 1H), 6.62 (s, 1H), 6.79-6.81 (m, 1H), 6.85-6.87 (m, 1H), 6.91-6.95 (m, 1H), 7.03-7.06 (m, 1H), 7.09-7.11 (m, 1H), 7.19-7.30 (m, 4H), 7.38 (br, 1H).

MS [(+)ESI, m/z]: 551 $[M+H]^+$.

Anal. Calcd. for $C_{34}H_{38}N_4O_3$+ 0.20 H_2O: C 73.67, H 6.98, N 10.11.

Found: C 73.50, H 7.08, N 9.96.

Example 12

7,8-Dimethoxy-[10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl][2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]methanone

Step A. 1-[(4,5-Dimethoxy-2-nitrophenyl)methyl]-1H-pyrrole-2-carboxaldehyde

To a suspension of sodium hydride (0.724 g, 60 % suspension in oil) in N,N-dimethyl formamide (50 mL) was added pyrrole 2- carboxaldehyde (1.7 g, 18.1 mmol) and the reaction mixture was stirred for 30 minutes. It was then cooled to 0 °C and 4,5-dimethoxy-2-nitrobenzyl bromide (5.0 g, 1 equiv) was added dropwise over 20 minutes. After the addition, the reaction mixture was stirred at room temperature for 3 hours. It

was then diluted with ethyl acetate (450 mL), washed with water, dried over anhydrous magnesium sulfate, filtered and evaporated to dryness. The crude product was triturated with water, filtered and washed with water. This material was dried over anhydrous potassium carbonate in vacuo to provide the title compound as a yellow crystalline solid (4.97 g), m.p. 109-112°C, which was used in the next step.

Step B. 7,8-Dimethoxy-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine

A mixture of the 1-[(4,5-dimethoxy-2-nitrophenyl)methyl]-1H-pyrrole-2-carboxaldehyde of Step A (4.97 g), acetic acid (0.5 mL), magnesium sulfate (0.5 g) and 10% palladium on charcoal (0.5 g) in ethyl acetate (50 mL) was hydrogenated overnight at atmospheric pressure. The reaction was then filtered through Celite and the solvent removed in vacuo to give the crude title compound as an amber foam (3.2 g) which was used in the next step without further purification.

Step C. 7,8-Dimethoxy-(10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl)-(4-bromo-3-methyl-phenyl)-methanone

To a solution of 7,8-dimethoxy-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine of Step B (3.20 g) in dichloromethane (20 mL) was added 3-methylbenzoyl chloride (3.4 g, 1.1 equiv) and triethylamine (2.0 g, 1.5 equiv) and the mixture was stirred at room temperature overnight. The solvent was then removed in vacuo and the residue chromatographed on silica gel eluting with a solvent gradient from 5 to 50% of ethyl acetate in petroleum ether to provide the title compounds as a yellow crystalline solid (3.5 g) , m.p. 165-168 °C.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.30 (s, 3H), 3.55 (br, 3H), 3.85 (s, 3H), 5.1 (br, 4H), 6.05 (br, 1H), 6.1 (t, 1H), 6.3 (br, 1H), 6.65 (t, 1H), 6.8 (s, 2H), 7.3 (s, 2H).

MS [(+)ESI, m/z]: 442 $[M + H]^+$.

Step D. 7,8-Dimethoxy-[10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl][2-methyl-2'-trifluoromethyl-[1,1']-biphenyl]-4-yl]methanone

The 7,8-dimethoxy-(10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl)-(4-bromo-3-methyl-phenyl)-methanone of Step C (1.0 g) was reacted with 2-trifluoromethylphenyl boronic acid (0.645 g, 1.5 equiv.), potassium phosphate (0.964 g, 2.0 equiv.) and a catalytic amount (0.050 g) of tetrakis(triphenylphosphine) palladium(0) in

refluxing dioxane (10 mL) under nitrogen for 24 hours. The reaction was then cooled to room temperature, filtered through Celite, and the solvent removed in vacuo. The residue was dissolved in dichloromethane and the solution was washed with water, dried over anhydrous magnesium sulfate, filtered and evaporated to dryness. The crude product so obtained was purified by chromatography on silica gel eluting with 5% ethyl acetate/dichloromethane to provide the title product (1.0 g) as a white crystalline solid, m.p. 187-188 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.85 (s, 3H), 3.40 (s, 3H), 3.70 (s, 3H), 5.20 (br, 4H), 5.92 (t, 1H), 5.96 (s, 1H), 6.56 (s, 1H), 6.77 (t, 1H), 6.90 (m, 1H), 7.05 (m, 2H), 7.20 (d, 1H), 7.30 (s, 1H), 7.58 (t, 1H), 7.68 (t, 1H), 7.80 (d, 1H).

MS [(+)APCI, m/z]: 507 $[M+H]^+$.

Anal. Calcd. for $C_{29}H_{25}F_3N_2O_3$: C 68.77, H 4.97, N 5.53. Found: C 68.85, H 5.05, N 5.43.

Example 13

N-Methyl-[N-(3-dimethylamino)propyl]-7,8-dimethoxy-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepine-3-carboxamide hydrochloride salt

A solution of the 7,8-dimethoxy-[10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-10-yl][2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]methanone of Example 12, Step D (0.31 mmol), diphosgene (1.1 equiv.) and triethylamine (1.5 equiv.) in dichloromethane (5 mL) was stirred at room temperature overnight. The solvent was removed in vacuo and the residue was dissolved in dichloromethane (5 mL). To the solution was added triethylamine (1.5 equiv.) and 3-(dimethylaminopropyl)-1-methyl amine (1.5 equiv.). The reaction mixture was then washed with water, dried over anhydrous magnesium sulfate, filtered and evaporated to dryness. The residue was first chromatographed on silica gel eluting with a solvent gradient from 2 to 5% of methanol in dichloromethane and then chromatographed again with solvent gradient from 2 to 5% of methanol in ethyl acetate to provide the title compound (0.100 g) as a colorless foam. Treatment of a solution of the free base in ethanol with anhydrous hydrogen chloride in dioxane followed by removal of the solvent provided the hydrochloride salt as a brown solid, m.p. 118°C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.85 (s, 3H), 2.00 (m, 2H), 3.05 (t, 2H), 2.75 (s, 6H), 3.10 (s, 3H), 3.40 (s, 3H), 3.55 (t, 2H), 3.70 (s, 3H), 5.30 (s, 4H), 6.05 (s, 1H), 6.35 (d, 1H), 6.50 (s, 1H), 6.90 (s, 1H), 6.95 (s, 2H), 7.20 (d, 1H), 7.30 (s, 1H), 7.60 (t, 1H), 7.70 (t, 1H), 7.80 (d, 1H), 10.25 (br, 1H).

MS [(+)ESI, m/z]: 649 $[M+H]^+$.

Anal. Calcd. For $C_{36}H_{39}F_3N_4O_4$+ HCl + $2H_2O$: C 59.95, H 6.15, N 7.77. Found: C 59.40, H 6.63, N 7.86.

Example 14

7,8-Dimethoxy-10-{[2-methyl-2'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl]carbonyl}-[(10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)carbonyl]-4-piperidinone

A solution of the 7,8-dimethoxy-[10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-10-yl][2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]methanone of Example 12, Step D (0.31 mmol), diphosgene (1.1 equiv.) and triethylamine (1.5 equiv.) in dichloromethane (5 mL) was stirred at room temperature overnight. The solvent was removed in vacuo, the residue was dissolved in dichloromethane (5 mL), and then triethylamine (1.5 equiv.) and 4-piperidone (1.5 equiv.) were added. The reaction mixture was stirred overnight, washed with water, dried over anhydrous magnesium sulfate, filtered and evaporated to dryness. The residue was first chromatographed on silica gel eluting with 2% methanol in dichloromethane and then chromatographed again with 2% methanol in ethyl acetate to provide the title compound as a yellow solid, m.p. 132-134°C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.85 (s, 3H), 2.45 (m, 4H), 3.40 (s, 3H), 3.65 (s, 3H), 3.90 (t, 4H), 5.20 (br, 2H), 5.35 (s, 2H), 6.10 (s, 1H), 6.40 (d, 1H), 6.50 (s, 1H), 6.90 (s, 1H), 7.00 (s, 1H), 7.05 (s, 1H), 7.20 (d, 1H), 7.30 (s, 1H), 7.60 (t, 1H), 7.65 (t, 1H), 7.80 (d, 1H).

MS [(+)APCI, m/z]: 632 $[M+H]^+$.

Anal. Calcd. for $C_{35}H_{32}F_3N_3O_5$ + H_2O: C 64.71, H 5.38, N 6.47.

Found: C 65.20, H 5.12,

N, 6.41.

Example 15

10-{[6-Chloro-3-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid

Step A . 4-Iodo-5-chloro-2-methoxy benzoic acid

A stirred solution of 4-amino-5-chloro-2-methoxy benzoic acid (12.25 g , 60.8 mmol) in water (136 mL) and concentrated sulfuric acid (34 mL) was cooled to 0 °C in a flask fitted with an overhead stirrer. A solution of sodium nitrite (4.62 g , 66.9 mmol) in water (26 mL) was added dropwise while keeping the internal temperature around 0 °C. Potassium iodide (11.11 g , 66.9 mmol) and iodine (4.246g , 33.5 mmol) were dissolved in water (130 mL) and added dropwise to the stirred reaction mixture. After 2 hours the reaction was extracted with ethyl acetate. The organic extracts were then washed with 10% sodium thiosulfate and brine, then dried over magnesium sulfate, filtered and evaporated to dryness to yield 11.32 g of the title compound, m.p. 150-151°C. This material was used in the next step without further purification.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 13.03 (br, 1H), 7.70 (s, 1H), 7.63 (s, 1H), 3.82 (s, 3H).

MS [(-)-APCI, m/z]: 311 $[M - H]^-$.

Anal. Calcd. for $C_8H_6ClIO_3$: C 30.75, H 1.94. Found: C 31.28, H 1.78.

Step B. 2-Chloro-2'-trifluoromethyl-5-methoxy[1,1'-biphenyl]-4-carboxylic acid.

To a stirred solution of 4-iodo-5-chloro-2-methoxy benzoic acid of Step A (3.12 g, 10 mmol) in N,N-dimethylformamide (100 mL) was added 2-trifluoromethyl phenyl boronic acid (5.70 g, 30 mmol) and potassium carbonate (12.73 g, 92 mmol). This mixture was purged with nitrogen and then treated with tetrakis(triphenylphosphine) palladium(0) (0.58 g, 0.5 mmol). The reaction was heated to reflux overnight, cooled, acidified with 2 N hydrochloric acid and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, filtered, and evaporated to provide a nearly quantitative amount of the title acid which was used in the next step without further purification.

Step C. 10-{[6-Chloro-3-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine

A stirred solution of the 2-chloro-2'-trifluoromethyl-5-methoxy [1,1'-biphenyl]-4-carboxylic acid of Step B (3.46 g, 10.46 mmol) in tetrahydrofuran (20 mL) containing a catalytic amount of N,N-dimethylformamide was treated dropwise with thionyl chloride (1.36 g, 11.51 mmol). The reaction mixture was stirred for 2 hours, and then added dropwise to a solution of 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine (1.92 g 10.46 mmol) in tetrahydrofuran (20 mL) containing triethylamine (2.32 g, 23 mmol). The reaction mixture was stirred for 2 hours, diluted with dichloromethane and washed with saturated aqueous sodium bicarbonate and brine. The organic layer was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. Trituration of the residue with acetone gave the title compound (3.14 g). Recrystallization from acetone/hexanes provided white crystals, m.p. 208-210°C;

^{1}H NMR (DMSO-d_6, 400 MHz) δ 3.46 (s, 3H), 5.16-5.20 (br d, 3H), 5.89 (t, 1H), 5.97 (s, 1H), 6.70 (s, 1H), 6.80 (t, 1H), 7.80-7.00 (m, 10H);

MS [(+) ESI, m/z]: 497 $[M+H]^+$.

Anal. Calcd. for $C_{27}H_{20}ClF_3N_2O_2$+ 0.5 H_2O: C 64.10, H 4.18, N 5.54. Found: C 64.40, H 3.97, N 5.54.

Step D. 10-{[6-Chloro-3-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid

A solution of the 10-{[6-chloro-3-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine of Step C (2.29 g, 4.6 mmol) in dichloromethane (30 mL) was treated with N,N-diisopropylethyl amine (0.62 g, 4.84 mmol) and stirred for 10 minutes. Trichloroacetyl chloride (0.92 g, 5.07 mmol) was then added dropwise. The reaction mixture was stirred overnight, diluted with dichloromethane, washed with 0.1 N hydrochloric acid, saturated aqueous sodium bicarbonate, and brine. The organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to yield the crude trichloroketone intermediate which without further purification, was dissolved in acetone and treated with an excess of 1N sodium hydroxide. The mixture was stirred overnight, and then diluted with isopropyl acetate and acidified with 1 N hydrochloric acid. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The

solid residue was triturated with methanol to provide the title compound (1.23g) as a white solid, m.p. 220-222°C (dec).

^{1}H NMR (DMSO-d_6, 400 MHz) δ 3.40 (s, 3H), 6.12 (d, 1H), 6.68 (s, 1H), 6.72 (d, 1H), 6.94 (s, 2H), 7.07 (t, 1H), 7.25 (d, 2H), 7.62 (t, 2H), 7.70 (t, 1H), 7.78 (d, 1H), 12.31 (br, 1H).

MS [(+)APCI, m/z]: 541 $[M+H]^+$.

Anal. Calcd. for $C_{28}H_{20}ClF_3N_2O_4$ + 0.25 H_2O: C 61.66, H 3.79, N 5.14.

Found: C 61.47, H 3.64, N 5.06.

Example 16

10-{[2'-Chloro-6-chloro-3-methoxy-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid

Step A. 2'-Chloro-2-chloro-5-methoxy-[1,1'-biphenyl]-4-carboxylic acid.

To a stirred solution of 4-iodo-5-chloro-2-methoxy benzoic acid (3.12 g, 10 mmol) in N,N-dimethylformamide (100 mL) was added 2-chloro phenyl boronic acid (5.07 g, 32.4 mmol) and potassium carbonate (12.73 g, 92 mmol). This mixture was purged with nitrogen and then treated with tetrakis(triphenylphosphine) palladium(0) (0.58 g, 0.5 mmol). The reaction was heated to reflux overnight, cooled, acidified with 2 N hydrochloric acid and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, filtered, and evaporated to provide a nearly quantitative amount of the title acid which was used in the next step without further purification.

Step B. 10-{[2'-Chloro-6-chloro-3-methoxy-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine

A stirred solution of the 2'-chloro-2-chloro-5-methoxy-[1,1'-biphenyl]-4-carboxylic acid of Step A (3.09 g, 10.46 mmol) in tetrahydrofuran (20 mL) containing a catalytic amount of N,N-dimethylformamide was treated dropwise with thionyl chloride (1.36 g, 11.51 mmol). The reaction mixture was stirred for 2 hours, and then added dropwise to a solution of 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine (1.92 g 10.46 mmol) in tetrahydrofuran (20 mL) containing triethylamine (2.32 g, 23 mmol). The reaction mixture was stirred for 2 hours, diluted with dichloromethane and washed with saturated

aqueous sodium bicarbonate and brine. The organic layer was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. Trituration of the residue with ethyl acetate gave the title compound (1.93 g) which was recrystallized from ethyl acetate/hexanes as white crystals, m.p. 209-211 °C;

^{1}H NMR (DMSO-d_6, 400 MHz) δ 3.55 (s, 3H), 5.16-5.20 (br m, 3H), 5.89 (t, 1H), 5.97 (s, 1H), 6.71 (s, 1H), 6.80 (s, 1H), 7.04-7.60 (m, 10H).

MS [(+) APCI, m/z]: 463 $[M+H]^+$.

Anal. Calcd. for $C_{26}H_{20}Cl_2N_2O_2$+ 0.25 $C_4H_8O_2$: C 66.81, H 4.57, N 5.77.

Found: C 66.76, H 4.24, N 5.93.

Step C. 10-{[2'-Chloro-6-chloro-3-methoxy-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid

A solution of 10-{[2'-chloro-6-chloro-3-methoxy-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine of Step B (2.1 g, 4.6 mmol) in dichloromethane (30 mL) was treated with N,N-diisopropylethyl amine (0.62 g, 4.84 mmol) and stirred for 10 minutes. Trichloroacetyl chloride (0.92 g, 5.07 mmol) was then added dropwise. The reaction mixture was stirred overnight, diluted with dichloromethane, washed with 0.1 N hydrochloric acid, saturated aqueous sodium bicarbonate, and brine. The organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to yield the crude trichloroketone intermediate which without further purification, was dissolved in acetone and treated with an excess of 1N sodium hydroxide. The mixture was stirred overnight, diluted with isopropyl acetate and acidified with 1 N hydrochloric acid. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The solid residue was triturated with methanol to provide the title compound as a white solid, which was used without further purification.

Example 17

10-{[6-Chloro-3-methoxy-2'-ethoxy[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine

Step A. 2-Chloro-2'-ethoxy-5-methoxy [1,1'-biphenyl]-4-carboxylic acid

To a stirred solution of 4-iodo-5-chloro-2-methoxy benzoic acid of Example 15, Step A (0.500 g, 1.6 mmol) in N,N-dimethylformamide (30 mL) was added 2-ethoxy phenyl boronic acid (0.8 g, 4.8 mmol) and potassium carbonate (2.04 g, 14.7 mmol). This mixture was purged with nitrogen and then treated with a catalytic amount of tetrakis (triphenylphosphine) palladium(0) (0.093 g, 0.08 mmol). The reaction was heated to reflux overnight, cooled, acidified with 2 N hydrochloric acid and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, filtered, and evaporated to yield the title acid which was used in the next step without further purification.

Step B. 10-{[6-Chloro-3-methoxy-2'-ethoxy-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine

To a stirred solution of the 2-chloro-2'-ethoxy-5-methoxy [1,1'-biphenyl]-4-carboxylic acid of Step A (0.491 g) in tetrahydrofuran (5 mL) containing a catalytic amount of N,N-dimethyl formamide was added dropwise thionyl chloride (0.210 g, 1.76 mmol). The reaction mixture was stirred for 2 hours, and then added dropwise to a solution of 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine (0.294 g, 1.60 mmol) in tetrahydrofuran (5 mL) containing triethylamine (0.357 g, 3.52 mmol). The reaction mixture was stirred for 2 hours, diluted with dichloromethane and washed with saturated aqueous sodium bicarbonate and brine. The organic layer was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. Trituration of the residue with methanol provided the title compound as an off-white solid, 99.24% pure by analytical HPLC [Primesphere C-18 column (2.0 x 150 mm); mobile phase 70/30 acetonitrile/water containing 0.1% phosphoric acid], m.p. 213-215 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.11, (t, 3H), 3.51 (s, 3H), 3.92 (q, 2H), 5.17-5.20 (br, m, 3H), 5.89 (t, 1H), 5.97 (s, 1H), 6.67-7.55 (m, 10H).

MS [(+)APCI, m/z]: 473 $[M+H]^+$.

Anal. Calcd. for $C_{28}H_{25}ClN_2O_3$: C 71.11, H 5.33, N 5.92. Found: C 70.31, H 5.27, N 5.79.

Example 18

10-{[6-Chloro-3-methoxy-2'-fluoro-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid

Step A. 2-Chloro-2'-fluoro-5-methoxy[1,1'-biphenyl]-4-carboxylic acid

To a stirred solution of 4-iodo-5-chloro-2-methoxy benzoic acid of Example 15, Step A (3.72 g, 19.1 mmol) in N,N-dimethylformamide (20 mL) was added 2-fluoro phenyl boronic acid (5.0 g, 35.7 mmol) and potassium carbonate (14.8 g, 107 mmol). This mixture was purged with nitrogen and then treated with a catalytic amount of tetrakis (triphenylphosphine) palladium(0) (0.688 g, 0.59 mmol). The reaction was heated to reflux overnight, cooled, acidified with 2 N hydrochloric acid and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was flash chromatographed on acid washed silica using a 10 to 50% gradient of diethyl ether in hexane to provide the desired title compound (3.8 g) as a white solid.

^{1}H NMR (DMSO-d_6, 400 MHz) δ 3.83 (s, 3H), 7.15 (s, 1H), 7.30-7.35 (m, 2H), 7.42 (m, 1H), 7.48-7.54 (m, 1H), 7.74 (s, 1H).

MS [(+)ESI, m/z]: 298 $[M+NH_4]^+$.

Anal. Calcd. for $C_{14}H_{10}ClFO_3$: C 59.91, H 3.59. Found: C 59.79, H 3.35.

Step B. 10-{[6-Chloro-3-methoxy-2'-fluoro-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine

To a stirred solution of 2-chloro-2'-fluoro-5-methoxy[1,1'-biphenyl]-4-carboxylic acid of Step A (3.80 g, 13.5 mmol) in tetrahydrofuran (20 mL) containing a catalytic amount of N,N-dimethylformamide was added dropwise thionyl chloride (1.77 g, 14.9 mmol). The reaction mixture was stirred for 2 hours, and then added dropwise to a solution of 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine (2.49 g, 13.5 mmol) in tetrahydrofuran (20 mL) containing triethylamine (3.0 g, 29.8 mmol). The reaction mixture was stirred for 2 hours, diluted with dichloromethane and washed with saturated aqueous sodium bicarbonate and brine. The organic layer was dried over

anhydrous magnesium sulfate, filtered, and evaporated to dryness. Recrystallization of the residue from ethyl acetate/heptane provided the title compound as a pale yellow solid, m.p. 192-194°C, found to be 99.99% pure by analytical HPLC [Primesphere C-18 column (2.0 x 150 mm); mobile phase: gradient from 10 to 100% of acetonitrile/water containing 0.1% phosphoric acid, 7 minute gradient].

^{1}H NMR (DMSO-d_6, 400 MHz) δ 3.55 (s, 3H), 5.19 (br m, 2H), 5.90 (t, 1H), 5.96 (s, 1H), 6.80 (s, 2H), 7.07-7.63 (m, 10H).

MS [(+)ESI, m/z]: 447 $[M+H]^+$.

Anal. Calcd. for $C_{28}H_{20}ClFN_2O_2+H_2O$: C 69.60, H 4.54, N 6.24.

Found: C 69.39, H 4.41, N 6.20.

Step C. 10-{[6-Chloro-3-methoxy-2'-fluoro-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid

A solution of the 10-{[6-chloro-3-methoxy-2'- fluoro-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine of Step B (3.02 g, 6.76 mmol) in dichloromethane (35 mL) was treated with N,N-diisopropylethyl amine (0.960 g, 7.43 mmol) and stirred for 10 minutes. Trichloroacetyl chloride (1.47 g, 8.10 mmol) was then added dropwise. The reaction mixture was stirred overnight, diluted with dichloromethane, washed with 0.1 N hydrochloric acid, saturated aqueous sodium bicarbonate, and brine. The organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to yield the crude trichloroketone intermediate which without further purification, was dissolved in acetone and treated with an excess of 1 N sodium hydroxide The mixture was stirred overnight, and then diluted with isopropyl acetate and acidified with 1 N hydrochloric acid. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The solid residue was triturated with methanol to provide the title compound (2.95 g) as a beige solid, m.p. 207-208°C.

^{1}H NMR (DMSO-d_6, 400 MHz) δ 3.49 (br, 3H), 6.12 (d, 1H), 6.72 (d, 1H), 6.77 (s, 1H), 7.01 (d, 2H), 7.09 (m, 1H), 7.26 (m, 4H), 7.45 (m, 2H), 7.61 (br, 1H), 12.35 (br, 1H).

MS [(+)APCI, m/z]: 491 $[M+H]^+$.

Anal. Calcd for $C_{27}H_{20}ClFN_2O_4$: C 66.06, H 4.11, N 5.71.

Found: C 65.68, H 4.24, N 5.48.

Example 19

10-{[2-Methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid

Step A. Trifluoromethanesulfonic acid 4-formyl-2-methoxy-phenyl ester

To a solution of vanillin (6.08 g, 40.0 mmol) and triethylamine (6.70 mL, 48.0 mmol) in dichloromethane (300 mL) was added dropwise a solution of trifluoromethane sulfonic anhydride (12.4 g, 44.0 mmol) in dichloromethane (100 mL) at 0 °C. After stirring for 2 hours, the solution was concentrated, and the residue washed with water and extracted twice with ethyl acetate. Upon drying and concentrating, the residual dark oil was subjected to flash chromatography on silica gel eluting with 20% ethyl acetate in hexane providing the title product (8.91 g) as a light yellow oil, which was used in the next step without further purification.

Step B. 2-Methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-carboxaldehyde

A stirred solution of trifluoromethanesulfonic acid 4-formyl-2-methoxy-phenyl ester of Step A (6.9 g, 22.1 mmol), 2-trifluoromethyl phenyl boronic acid (5.4 g, 28.6 mmol) and potassium phosphate (13.2 g, 62.2 mmol) in N,N-dimethylformamide (120 mL) was degassed with nitrogen, whereupon a catalytic amount (0.285 g) of [1,4-bis-(diphenylphosphine)butane]palladium (II) dichloride was added. The solution was heated to 120 °C for 5 hours, poured into water and extracted with ethyl acetate. The combined extracts were washed with water, dried over anhydrous magnesium sulfate and filtered through a plug of silica gel. Removal of the solvent provided the crude title compound (4.54 g) as an oil, which was used as such in the next step.

^{1}H NMR (200 MHz, $CDCl_3$): δ 10.03 (s, 1H), 8.14 (d,1H), 7.31-7.56 (m, 6H), 3.91 (s, 3H).

Step C. 2-Methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-carboxylic acid

The 2-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-carboxaldehyde of Step B (0.95 g, 3.41 mmol) and sulfamic acid (0.43 g, 4.43 mmol) were dissolved in a mixture of tetrahydrofuran and water (1:1, v/v, 30 mL). Sodium chlorite (0.31 g, 4.43 mmol) was added under stirring, and the solution turned yellow. After 30 minutes, additional sodium chlorite and sulfamic acid were added, and the solution stirred an additional hour. The

solution was then concentrated, and the residue partitioned between ethyl acetate and water. The ethyl acetate layer was dried and concentrated to yield an oil, which solidified upon trituration with hexane to provide the title compound (0.84 g) as a yellow solid, which was used in the next step.

Step D. (10,11-Dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl)- (2-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)-methanone

The 2-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-carboxylic acid of step C (1.6 g, 5.40 mmol) was added to a flask containing toluene (30 mL), thionyl chloride (1.4 mL) and one drop of N,N-dimethylformamide. The solution was stirred at 70 °C for 1 hour and then concentrated in vacuo. The residue was diluted with dichloromethane (40 mL) and to this solution was added 10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine (0.94 g, 5.16 mmol). After the solution became homogeneous, N,N-diisopropylethyl amine (1.07 mL, 6.19 mmol) was added in one portion at 0 °C. After 30 minutes the solution was concentrated, and the residue partitioned between water and ethyl acetate. The ethyl acetate was dried and concentrated to give a crude oil, which was chromatographed on silica gel eluting with 30% ethyl acetate in hexane to yield 1.2 g of product. The solid was recrystallized from ethyl acetate/ hexane to provide the desired title product (0.87 g) as colorless crystals, m.p. 146-148 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, 1H), 7.62 (t, 1H), 7.53 (t, 1H), 7.46 (d, 1H), 7.19 (m, 2H), 7.11 (t,1H), 6.92-7.01 (m, 4H), 6.83 (s, 1H), 5.95 (bs, 1H), 5.91 (s, 1H), 5.31 (br, 4H), 3.45 (s, 3H).

MS [(+)ESI, m/z]: 463 $[M+H]^+$.

Anal. Calcd. for $C_{27}H_{21}F_3N_2O_2$: C 70.12, H 4.58, N 6.06. Found: C 70.53, H 4.72, N 5.89.

Step E. 10-{[2-Methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid

To a stirred solution of the (10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl)- (2-methoxy-2'- trifluoromethyl-[1,1'-biphenyl]-4-yl)-methanone of Step D (2.34 g, 5.0 mmol) and N,N-diisopropylethyl amine (1.04 mL, 6.0 mmol) in dichloromethane (100 mL) was added dropwise a solution of trichloroacetyl chloride (1.09 g, 6.0 mmol) in dichloromethane (20 mL) kept at 0 °C. After the addition was complete, the solution was stirred overnight at room temperature, then washed with 10% aqueous potassium

carbonate. The organic phase was dried and concentrated to yield a black residue. The residue was purified by filtration through a plug of silica gel, eluting with 20% ethyl acetate in hexane. The resulting tan colored product was dissolved in acetone and 1 N sodium hydroxide (2:1, v/v) and the mixture was stirred for 30 minutes. The solution was then concentrated and extracted with ethyl acetate. The combined organic phases were dried and concentrated to yield a yellow oil. The oil was triturated with hexane, and the resulting solid was removed by filtration to yield the title compound (1.86 g) as an off white solid, which was used without further purification.

Example 20

{[10-(2-Methoxy)-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-[(2S)-[(2-pyrrolidin-1-yl)methyl]pyrrolidin-1-yl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl-methanone

To a stirred solution of the 10-{[2-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid of Example 19 (0.230 g, 0.5 mmol) in N,N-dimethylformamide (15 mL), was added 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (0.120 g, 0.625 mmol) and 1-hydroxybenzotriazole (0.087 g, 0.625 mmol). After the solution became homogeneous, (S)-(+)-1-[(2-pyrrolidin-1-yl)methyl]-pyrrolidine (0.100 g, 0.625 mmol) was added, and the mixture was stirred at room temperature overnight. The solution was then poured into water and extracted with ethyl acetate. The combined ethyl acetate layers were washed with water, dried over anhydrous sodium sulfate and concentrated to dryness. The residue was subjected to silica chromatography eluting with 5% methanol in chloroform. The pure fractions were concentrated and the residue triturated several times with hexane to provide the title product (0.120 g) as a white solid, m.p. 125-128°C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.74 (d,1H), 7.62 (t,1H), 7.56 (t, 1H), 7.38 (m, 1H), 7.19 (d, 1H), 7.11 (t,1H), 7.04 (t, 1H), 6.85-6.973 (m, 4H), 6.40 (s,1H), 6.06 (s,1H), 5.62 (br, 1H), 5.46 (br, 1H), 4.35 (br, 1H), 3.57 (m,2H), 1.4-1.98 (m, 8H).

MS [EI, m/z]: 642 $[M]^+$.

Anal. Calcd. for $C_{37}H_{37}F_3N_4O_3 + 0.5\ H_2O$: C 68.19, H 5.88, N 8.60.

Found: C 68.38, H 6.15, N 8.20.

Example 21

N-Methyl-[N-(3-dimethylamino)propyl]-10-{[2-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-3-carboxamide

The title compound (white solid, m.p. 140-142 °C) was prepared by coupling the 10-{[2-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid of Example 19, with 3-(dimethylamino)-propyl-1-methylamine (1.25 equiv), in the manner of Example 20.

^{1}H NMR (400 MHz, DMSO-d_6): δ 1.65 (m, 2H), 2.05–2.21 (m, 8H), 3.06 (s, 3H), 3.42 (s, 3H), 3.44 (t, 2H), 5.20 (br, 2H), 5.44 (br, 2H), 6.06 (s, 1H), 6.23 (s,1H), 6.85-6.97 (m, 4H), 7.04 (t, 1H), 7.11 (t, 1H), 7.19 (d, 1H), 7.38 (d, 1H), 7.56 (t, 1H), 7.62 (t, 1H), 7.74 (d, 1H).

MS [EI, m/z]: 604 $[M]^+$.

Anal. Calcd. for $C_{34}H_{35}F_3N_4O_3$: C 67.54, H 5.83, N 9.27. Found: C 67.15, H 5.82, N 9.20.

Example 22

N-Methyl-[N-(2-dimethylamino)ethyl]-10-{[2-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

The title compound (white solid, 0.149 g, m.p. 187-190°C) was prepared by coupling the 10-{[2-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid of Example 19, with 3-(dimethylamino)ethyl-1-methyl amine (1.25 equiv), in the manner of Example 20.

^{1}H NMR (400 MHz, DMSO-d_6): δ 3.06 (s, 3H), 3.42 (m,5H), 3.84 (t, 2H), 5.54 (br, 2H), 6.06 (s,1H), 6.42 (s,1H), 6.85-6.97 (m, 4H), 7.04 (t, 1H), 7.11 (t,1H), 7.19 (m, 2H), 7.38 (d, 1H), 7.56 (t, 1H), 7.62 (t,1H), 7.74 (d,1H).

MS [EI, m/z]: 590 $[M]^+$.

Anal. Calcd. for $C_{33}H_{33}F_3N_4O_3$: C 63.21, H 5.46, N 8.93. Found: C 62.15, H 5.59, N 8.28.

Example 23

[4-(Naphtalen-1-yl)phenyl][10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl]methanone

Step A. 4-Naphthalen-1-yl-benzoic acid methyl ester

Methyl 4-bromobenzoate (0.96 g, 4.46 mmol) was added to a mixture of 1-naphthaleneboronic acid (0.73 g, 4.25 mmol) and sodium carbonate (0.075 g, 7.08 mmol) in toluene (30 mL), ethanol (6 mL) and water (12 mL). The resultant solution was purged with nitrogen for 10 minutes before tetrakis(triphenylphosphine)palladium(0) (0.10 g, 0.09 mmol) was added. The reaction mixture was heated to reflux for 65 hours. The solution was cooled to ambient temperature, then filtered through a pad of Celite, which was subsequently rinsed with ethyl acetate. The combined filtrate was diluted to 100 mL with water/ethyl acetate (1:1). The aqueous layer was extracted with ethyl acetate, and the combined extracts were dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness to yield the title compound as a gold oil (1.09 g). This material was used without further purification in the next step.

^{1}H NMR (300MHz, DMSO-d_6): δ 3.92 (s, 3H), 7.57 (m, 6H), 7.75 (d, 1H), 8.02 (t, 2H), 8.10 (d, 2H).

Step B. 4-Naphthalen-1-yl-benzoic acid

To a stirred solution of the 4-naphthalen-1-yl-benzoic acid methyl ester of Step A (1.09 g, 4.15 mmol) in methanol (18 mL) and water (6 mL), cooled to 5°C, was added lithium hydroxide monohydrate (0.42 g, 10.0 mmol). The solution was allowed to warm to ambient temperature as stirring was continued for 20 hours. The reaction mixture was poured into water, acidified to pH 4 with acetic acid, and the resultant precipitate was isolated by vacuum filtration to afford the title compound as an off-white solid (0.92 g), m.p. 221-224 °C.

^{1}H NMR (400MHz, DMSO-d_6): δ 6.40-7.60 (m, 6H), 7.56 (d, 1H), 7.98 (d, 1H), 8.01 (d, 1H), 8.07 (d, 2H).

MS [EI, m/z]: 248 $[M]^+$.

Anal. Calc'd. for $C_{17}H_{12}O_2$: C 82.24, H 4.87. Found: C 81.90, H 4.63.

Step C. [4-(Naphtalen-1-yl)phenyl][10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl]methanone

N,N-Dimethylformamide (2 drops) was added to a solution of the 4-naphthalen-1-yl-benzoic acid of Step B (0.60 g, 2.40 mmol), in anhydrous tetrahydrofuran (15 mL) followed by oxalyl chloride (0.34 g, 2.64 mmol) and the mixture was warmed to reflux. The resultant solution was cooled to ambient temperature before being evaporated to dryness to give the crude acid chloride as a gold solid, which was used without further purification. To a mixture of 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine (0.37 g, 2.00 mmol) and triethylamine (0.24 g, 2.40 mmol) in dichloromethane (5 mL), cooled in an ice bath, was added dropwise a solution of the crude acid chloride in dichloromethane (5 mL). The cooling bath was removed and after stirring for 48 hours, the reaction mixture was washed sequentially with water, saturated aqueous sodium bicarbonate, saturated aqueous sodium chloride and 1 N sodium hydroxide. The dichloromethane solution was dried with anhydrous magnesium sulfate, filtered, then evaporated to dryness to yield a brown foam. Purification by flash chromatography on silica gel eluting with hexane-ethyl acetate (4:1) resulted in a white foam (0.47 g). Treatment of the white foam with diethyl ether and sonication resulted in a white solid (0.37g), m.p. 169.5-171 °C.

^{1}H NMR (400MHz, DMSO-d_6): δ 5.32 (br, 4H), 5.93 (m, 1H), 5.97 (s, 1H), 6.83 (m, 1H), 7.01 (d, 1H), 7.18 (m, 2H), 7.32 (t, 2H), 7.41, (d, 1H), 6.45-7.60 (m, 5H), 7.93 (d, 1H), 7.97 (d, 1H).

MS [EI, m/z]: 414 $[M]^+$.

Anal. Calcd. for $C_{29}H_{22}N_2O + 0.4\ H_2O$: C 82.60, H 5.45, N 6.64.

Found: C 82.71, H 5.44, N 6.54.

Example 24

[2-Chloro-4-(naphthalen-1-yl)phenyl][10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-10-yl]methanone

Step A. (4-Bromo-2-chloro-benzoyl)-10,11-dihydro-5H-pyrrolo [2,1-c][1,4]

N,N-Dimethylformamide (1 drop) was added to a solution of 4-bromo-2-chlorobenzoic acid (2.20 g, 9.35 mmol) in anhydrous tetrahydrofuran (20 mL). Oxalyl chloride (1.46 g, 11.46 mmol) was added and the mixture was warmed to reflux. The

resultant solution was cooled to ambient temperature before being evaporated to dryness to give the crude acid chloride as a gold viscous liquid, which was used without further purification. To a mixture of 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine (1.44 g, 7.79 mmol) and triethylamine (0.95 g, 9.35 mmol) in dichloromethane (40 mL) cooled in an ice bath, was added dropwise a solution of the acid chloride in dichloromethane (20 mL). The cooling bath was removed and after stirring for 22 hours, the reaction mixture was washed sequentially with water, saturated aqueous sodium bicarbonate, 0.5 N hydrochloric acid and water. The dichloromethane solution was dried over anhydrous sodium sulfate, filtered, then evaporated to dryness to yield an off-white foam. Purification by flash chromatography on silica gel eluting with hexane-ethyl acetate (2:1) resulted in a white foam (3.02 g), m.p. 77-80 °C. This material was used as is in the next step.

^{1}H NMR (400MHz, DMSO-d_6): δ 5.45 (br, 4H), 7.02 (t, 1H), 7.07 (td, 1H), 7.14 (td, 1H), 7.32 (br, 1H), 7.38 (d, 2H), 7.68 (br ,1H).

MS [EI, m/z]: 400 $[M]^+$.

Anal. Calcd. for $C_{19}H_{14}BrClO$: C 56.81, H 3.51, N 6.97. Found: C 56.30, H 3.32, N 6.75.

Step B. [2-Chloro-4-(naphthalen-1-yl)-phenyl]-(10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl)-methanone

1-Naphthaleneboronic acid (0.52 g, 3.00 mmol) was added to a mixture (4-bromo-2-chloro-benzoyl)-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine of Step A (1.27 g, 3.15 mmol) and sodium carbonate (0.53 g, 4.98 mmol) in toluene (22.5 mL), ethanol (4.5 mL) and water (9 mL). The resultant solution was purged with nitrogen for 10 minutes, then tetrakis(triphenylphosphine)palladium (0.18 g, 0.06 mmol) was added. The reaction mixture was heated to reflux for 76 hours. The solution was cooled to ambient temperature, then filtered through a pad of Celite, which was subsequently rinsed with ethyl acetate. The combined filtrate was diluted to 100 mL water/ethyl acetate (1:1). The aqueous layer was extracted with ethyl acetate, and the combined organic layer was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness to yield a brown oil. Purification by flash chromatography on silica gel eluting with hexane-ethyl acetate (5:1) resulted in a white solid which was dried under vacuum (0.62 g), m.p. 115-117.5 °C.

^{1}H NMR (400MHz, DMSO-d_6): δ 5.91 (t, 1H), 6.02 (br, 1H), 6.84 (br,1H), 7.14 (m, 2H), 7.24 (d, 1H), 7.34, (d, 1H), 7.95 (d, 1H), 7.98 (d, 1H).

MS [(+)ESI, m/z]: 449 $[M+H]^+$.

Anal. Calcd. for $C_{29}H_{21}ClN_2O$ + 0.25 H_2O: C 76.72, H 4.79, N 6.17.

Found C 76.72, H 4.53, N 5.95.

Example 25

[4-(4-Methyl-naphthalen-1-yl)phenyl][10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-10-yl]methanone

Step A. 4-(4-Methyl)-napthalen-1-yl-benzoic acid

To a mixture of 1-bromo-4-methyl napthalene (1.11 g, 5.00 mmol) and 4-carboxyphenyl boronic acid (1.00 g, 6.00 mmol) in ethylene glycol dimethyl ether (20 mL) was added a solution of sodium carbonate (2.37 g, 22.38 mmol) in water (18.75 mL). The resultant mixture was purged with nitrogen for 20 minutes before tetrakis (triphenylphosphine) palladium(0) (0.03 g, 0.02 mmol) was added. The reaction mixture was heated to reflux for 68 hours. After the solution cooled to ambient temperature, the solvent was removed in vacuo and the residue was acidified with 5 N hydrochloric acid to produce an orange-brown solid that was isolated by vacuum filtration. This material was used without further purification in the next step.

^{1}H NMR (300MHz, DMSO-d_6): δ 2.70 (s, 3H), 7.57 (d, 2H), 8.07 (d, 2H).

Step B. [4-(4-Methyl-naphthalen-1-yl)phenyl][10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-10-yl]methanone

N,N- Dimethylformamide (2 drops) was added to a solution of 4-(4-methyl)-napthalen-1-yl-benzoic acid of Step A (0.90 g, 3.43 mmol) in anhydrous tetrahydrofuran (10 mL). Oxalyl chloride (0.52 g, 4.12 mmol) was added and the mixture was warmed to reflux. The resultant solution was cooled to ambient temperature before being evaporated to dryness to give the crude acid chloride as a brown residue, which was used without further purification. To a mixture of 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine (0.53 g, 2.86 mmol) and triethylamine (0.35 g, 3.43 mmol) in dichloromethane (10 mL) cooled in an ice bath was added dropwise a solution of the crude acid chloride in dichloromethane (10 mL). The cooling bath was removed and

after stirring for 137 hours, the reaction mixture was washed sequentially with water, saturated aqueous sodium bicarbonate, and saturated aqueous sodium chloride. The dichloromethane solution was dried over anhydrous magnesium sulfate, filtered, then evaporated to dryness to yield an amber oil. Purification by flash chromatography on silica gel eluting with hexane-ethyl acetate (4:1) resulted in a tan foam (0.49 g). Treatment of this material with diethyl ether and sonication resulted in an off-white solid (0.37 g), m.p. 160-162 °C.

^{1}H NMR (400MHz, DMSO-d_6): δ 2.66 (s, 3H), 5.32 (br, 4H), 5.93 (t,1H), 5.97(br, 1H), 6.83 (t, 1H), 7.01 (d, 1H), 7.22 (d, 2 H), 7.28 (d, 2H), 7.39 (t, 3H), 7.45 (m, 2H), 7.57 (m, 2H), 8.06 (d, 1H).

MS [(+)ESI, m/z]: 429 $[M+H]^+$.

Anal. Calcd. for $C_{30}H_{24}N_2O$ + 0.13 H_2O: C 83.63, H 5.67, N 6.50.

Found: C 83.63, H 5.64, N 6.43.

Example 26

Methyl 10-{[2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1.4] benzodiazepine-8-carboxylate

Step A. [4-(2-Formyl-1H-pyrrole-1-yl)methyl]-3-nitro]-benzoic acid methyl ester

To a suspension of sodium hydride (8.1 g, 60 % suspension in oil) in N,N-dimethylformamide (25 mL) was added dropwise over 15 minutes a solution of pyrrole 2-carboxaldehyde (9.1 g, 1 equiv.) in N,N-dimethylformamide (25 mL). After the addition, the reaction mixture was stirred for 30 minutes and then cooled to 0 °C. A solution of 4-bromomethyl-2-nitrobenzoic acid (25.0 g, 1 equiv.) in N,N-dimethyl formamide (50 mL) was added dropwise over 20 minutes. After the addition, the reaction mixture was stirred at room temperature for 1 hour and then iodomethane (1.2 eq.) was added. The reaction mixture was stirred at room temperature overnight and diluted with water (200 mL). The solid was filtered, washed with water and dried over anhydrous potassium carbonate in vacuo at 50 °C to provide the crude title compound as a brown solid (26 g).which was used as such in the next step.

Step B. 10,11-Dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-8-carboxylic acid methyl ester

To a stirred solution of tin(II) chloride dihydrate (23 g, 3.5 eq) in 2 N hydrochloric acid (106 mL) was added the [4-(2-formyl-1H-pyrrole-1-yl)methyl]-3-nitro]-benzoic acid methyl ester of Step A (8 g). Methanol (200 mL) was then added to this solution and the reaction mixture was stirred at 40 °C for 2 hours. The reaction was then cooled to room temperature, quenched by the addition of saturated aqueous sodium carbonate (20 mL) and filtered through Celite. The filter pad was washed with methanol and hot ethyl acetate. The filtrate and washings were combined, concentrated in vacuo to a volume of 300 mL and extracted with ethyl acetate. The combined extracts were dried over anhydrous magnesium sulfate, filtered and concentrated in vacuo to a volume of 200 mL. Acetic acid (1 g) and 10% palladium on charcoal (1.5 g) were added and the mixture was hydrogenated overnight at atmospheric pressure. The reaction was then filtered through Celite and the solvent removed in vacuo to give a dark brown crystalline solid (16.4 g). This was dissolved in dichloromethane and filtered through a silica pad eluting with dichloromethane to provide the title compound as a yellow crystalline solid (11.7 g). Recrystallization from 1,2-dichloroethane yielded a yellow crystalline solid (5.7 g), m.p. 198-200 °C.

^{1}H NMR($CDCl_3$, 200 MHz): δ 3.95 (s, 3H), 4.50 (s, 2H), 5.20 (s, 2H), 6.05 (t, 2H), 6.70 (t, 1H), 7.05 (d, 1H), 7.15 (s, 1H), 7.20 (d, 1H), 7.30 (s, 1H).

Step C. Methyl 10-{[2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-8-carboxylate

To a solution of 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-8-carboxylic acid methyl ester of Step B (1.64 g) in 1,2-dichloroethane (25 mL) was added 4-(2-trifluoromethylphenyl)-3-methylbenzoyl chloride (2.0 g, 1.1 eq) prepared in the manner of Example 1, Step D and triethylamine (1.0 g) and the mixture was stirred at room temperature overnight. The solvent was then removed in vacuo and the residue chromatographed on silica gel eluting with 10% ethyl acetate in petroleum ether to provide the title compound as a white crystalline solid, m.p. 180-182 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.80 (s, 3H), 3.70 (s, 3H), 5.0-5.5 (br, 4H), 5.80 (t, 1H), 6.00 (s, 1H), 6.85 (t, 1H), 6.90 (s, 1H), 7.00 (br, 1H), 7.20 (d, 1H), 7.35 (s, 1H), 7.60 (t, 2H), 7.70 (t, 2H), 7.75 (d, 1H), 7.80 (d, 1H).

MS [(+)ESI, m/z]: 505 $[M+H]^+$.

Anal. Calcd. for $C_{29}H_{23}F_3N_2O_3$: C, 69.04; H, 4.60; N, 5.55.

Found: C, 67.76; H, 4.30; N, 5.40.

Example 27

[4-(2,5-Dimethyl-1-H-pyrrol-1-yl)-3-methoxy-phenyl] [10,11-dihydro-5H-pyrrolo[2,1-c][1,4] benzodiazepin-10-yl] methanone

A solution of (4-amino-3-methoxy-phenyl)[10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-10-yl]methanone prepared in the manner of Albright et al., E.P.636625-A2 (0.675g, 2 mmol) and acetonyl acetone (0.3mL, 2.5 mmol) in benzene (100 mL) was treated with a crystal of para-toluenesulfonic acid. The stirred solution was warmed to reflux for 46 hrs using a Dean Stark trap. The reaction was cooled to room temperature, diluted with dichloromethane (100 mL), washed with saturated aqueous sodium bicarbonate then water. The residue (oil, 0.900 g) was flash chromatography on silica gel eluting with 20% ethyl acetate in hexane to yield 0.610 g of the title compound as a white foam. Recrystallization of a sample of this material yielded yellow crystals, m.p. 141-144 °C.

^{1}H NMR (400MHz, DMSO-d_6): δ 1.72 (s, 6H), 3.52 (s,3H), 5.33 (br, 4H), 5.69 (s, 3H), 5.93 (t, 1H), 5.97 (br, 1H), 6.82(t, 1H),. 6.96 (q, 3H), 7.06 (t, 1H), 7.17 (t, 1H), 7.45 (d, 1H),

MS [(+)ESI m/z]: 412 $[M+H]^+$.

Anal. Calcd. for $C_{26}H_{25}N_3O_2$: C 75.89, H 6.12, N 10.12. Found: C 75.89, H 5.95, N10.15.

Example 28

[6-(Naphthalen-1-yl)-pyridin-3-yl]-[10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl]methanone

Step A. (6-Chloro-pyridin-3-yl)-[10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-10-yl]methanone

A solution of 10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine (100 mmol) and N,N-diisopropylethyl amine (130 mmol) in dichloromethane (500 mL) was cooled to 0 °C. 6-Chloronicotinoyl chloride (130 mmol) was added dropwise under nitrogen. The solution was stirred for one hour as it returned to room temperature. The reaction mixture was

filtered through a sica gel pad, washed with 0.5 N sodium hydroxide and water, dried over anhydrous magnesium sulfate. The solution was again filtered through a silica gel pad and evaporated to dryness in vacuo. The residual oil crystallized from diethyl ether to provide the title compound as a colorless crystalline solid, m.p. 165-167 °C.

^{1}HNMR 9400 Mhz, DMSO-d_6): δ 5.35 (br, 4H), 5.91 (t, 1H), 5.97 (s, 1H), 6.83 (t, 1H), 7.0 (br d, 1H), 7.18 (t, 1H), 7.19 (t, 1H), 7.39 (d, 1H), 7.46 (dd, 1H), 7.71 (d, 1H), 8.26 (s, 1H).

MS [EI, m/z]: 323 $[M]^+$.

Anal. Calcd. for $C_{18}H_{14}ClN_3O$: C 66.77, H 4.36, N 12.98.

Found: C 65.91, H 4.18, N 12.69.

Step B. [6-(Naphthalen-1-yl)-pyridin-3-yl]-[10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-10-yl]methanone

A suspension of (6-chloro-pyridin-3-yl)-[10,11-dihydro-5H-pyrrolo{2,1-c][1,4]-benzodiazepin-10-yl]methanone of Step A (0.645 g, 1.9 mmol) and naphthalene boronic acid (0.372 g, 2.1 mmol) in a mixture of toluene (1.2mL), ethanol (2mL) and 1M aqueous sodium carbonate (0.4mL) was sparged with nitrogen for 10 minutes. To this was added palladium(I) acetate (0.026 g, 0.1 mmol). The mixture was heated at reflux under a static pressure of nitrogen for 48 hrs. The reaction was diluted with ethyl acetate and water. The organic layer was washed with saturated aqueous sodium bicarbonate then water. The sample was dried over anhydrous magnesium sulfate, filtered and concentrated in vacuo to a brown oil. Flash chromatography of the residue on silica gel eluting with 20-50% ethyl acetate in hexane, yielded 0.180 g of a solid which was recrystallized from chloroform to provide the title compound as off white crystals, m.p. 155-158 °C.

^{1}H NMR (400MHz, DMSO-d_6): δ 5.40 (br, 4H), 5.93(m, 1H), 5.99 (s, 1H), 6.84 (s, 1H), 7.08(br d, 1H), 7.16 (t, 1H), 7.23 (t, 1H), 7.52 (m, 6H), 7.84(d, 2H), 7.98 (dd, 2H), 8.55 (s, 1H).

MS [(+)ESI, m/z]: 416 $[M+H]^+$.

Anal. Calcd. for $C_{28}H_{21}N_3O$ + 0.5 H_2O: C 79.22, H 5.23, N 9.90.

Found: C 79.08, H 4.94, N 9.73.

Example 29

(6-Phenyl-pyridin-3-yl)-[10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl]methanone

The title compound was prepared in the manner of Example 28 using phenyl-boronic acid (0.269 g), (6-chloro-pyridin-3-yl-[10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-10-yl]methanone of Example 28, Step A (0.645 g) and palladium(I) acetate (0.017g), in a mixture of toluene (12mL), 1M aqueous sodium carbonate (4mL) and ethanol (2mL). The initially obtained foam (0.387 g) was purified by HPLC (Primesphere C18, 5x25cm column eluting with 55% acetonitrile in water containing 0.1% formic acid) to yield the title product (0.200 g) as a yellow solid. Recrystallization of a sample from acetone/hexane yielded yellow needles, m.p. 171-174 °C.

^{1}H NMR (400MHz, DMSO-d_6): δ 5.37 (br, 4H), 5.92 (t, 1H), 5.97 (s, 1H), 6.83 (t, 1H), 7.03 (d, 1H), 7.10 (t, 1H), 7.18 (t, 1H), 7.46 (m, 4H), 7.73(d, 1H), 7.85 (d, 1H), 8.03 (dd, 2H), 8.44 (s,1H).

MS [(+)ESI, m/z]: 366 $[M+H]^+$.

Anal. Calcd. for $C_{24}H_{19}N_3O$ + 0.25 H_2O: C 77.92, H 5.31, N 11.36.

Found: C 77.70, H, 5.23, N 11.39.

Example 30

[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3,5-dimethyl-phenyl][10,11-dihydro-5H-pyrrolo[2,1-c][1,4] benzodiazepin-10-yl]methanone

Step A. Methyl 4-(2,5-dimethyl-1H-pyrrol-1-yl)-3,5-dimethylbenzoate

Methyl 4-amino-3,5-dimethylbenzoate [prepared in the manner of Chang et al., WO Patent 9631492 A1] (1.24g, 6.9 mmol), was converted into the title compound (1.55 g) in the manner of Example 27. Recrystallization from aqueous methanol yielded a white solid, m.p. 104-106 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.95 (s, 6H), 2.00 (s, 6H), 3.95 (s, 3H), 5.95 (br, 2H), 7.85 (s, 2H).

Step B. 4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3,5-dimethylbenzoic acid

Methyl 4-(2,5-dimethyl-1H-pyrrol-1-yl)-3,5-dimethylbenzoate of Step A (1.55g, 6 mmol) was dissolved in ethanol (100 mL) and treated with 1M sodium hydroxide (9 mL). The solution was refluxed overnight, cooled to room temperature, acidified with 1N hydrochloric acid, and diluted into water and ethyl acetate. The organic layer was washed with water until neutral, dried with anhydrous sodium sulfate, filtered and evaporated in vacuo to yield the title compound as a a cream colored solid (1.36 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.87 (s, 6H), 2.00 (s, 6H), 5.95 (s, 2H), 7.90 (s, 2H).

Step C. [4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3,5-dimethyl-phenyl][10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-10-yl]methanone

A solution of 4-(2,5-dimethyl-1H-pyrrol-1-yl)-3,5-dimethylbenzoic acid of Step B (0.495 g, 2 mmol) was dissolved in tetrahydrofuran (10 mL) and treated with N,N-dimethylformamide (10 µL) followed by oxalyl chloride (250 µL, 2.85 mmol) added dropwise to control gas evolution. When the gas evolution subsided, the solution was warmed to reflux for 5 minutes. The solution was then concentrated in vacuo, the residue was dissolved in tetrahydrofuran and evaporated to dryness. The residue was redissolved in dichloromethane and the solution added dropwise to a cold solution (0 °C) of 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine (0.372mg, 2 mmol) and Hünig's base (0.5mL) in dichloromethane. The solution was stirred overnight at room temperature, washed successively with 1N hydrochloric acid, saturated aqueous bicarbonate, and brine. The sample was then dried over anhydrous sodium sulfate, filtered and evaporated in vacuo to a yellow foam (0.75 g). Flash chromatography of this material on silica gel eluting with a solvent gradient of 10 to 20% of ethyl acetate in hexane, provided a white solid (0.130 g). Recrystallization of this material from ethyl acetate/hexane provided the title compound (0.120 g) as flat crystals, m.p. 197-199 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.75 (s, 3H), 1.77 (s, 3H), 5.18 (br, 4H), 5.89 (s, 2H), 6.05 (br, 1H), 6.08 (t, 1H), 6.69 (t, 1H), 6.85 (br, 1H), 7.03 (br, 3H), 7.16 (t, 1H), 7.35 (d, 1H). MS [(+)APCI, m/z]: 410 $[M+H]^+$.

Anal. Calcd. for $C_{27}H_{27}N_3O$ + 0.25 H_2O: C 78.33, H 6.69, N 10.15.
Found: C 78.04, H 6.53, N 10.08.

Example 31

[3-Methyl-4-(4-pyridinyl)phenyl]-[10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-10-yl]methanone

Step A. (4-Bromo-3-methylphenyl)[10,11-dihydro-5H-pyrrolo[2,1c][1,4]benzodiazepin-10-yl]methanone

A solution of 4-bromo-3-methyl benzoic acid (4.3 g, 2 mmol) in dry tetrahydrofuran (100 mL) was cooled to 0 °C under nitrogen. To this was added N,N-dimethylformamide (50 µL) followed by oxalyl chloride (2.2 mL, 25mmol) dropwise to control the gas evolution. When the gas evolution ceased, the mixture was warmed to reflux for 5 minutes then cooled to room temperature and concentrated in vacuo. The sample was treated with tetrahydrofuran and evaporated to dryness (twice) to yield the crude acid chloride as an orange oil. A solution of 10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine (3.60g, 20 mmol) and Hünig's base (4.35 mL, 25 mmol) in dichloromethane was cooled to 0 °C, and a solution of the crude acid chloride in dichloromethane (25 mL) was added dropwise. The mixture was stirred overnight at room temperature, washed with 1N hydrochloric acid, saturated aqueous sodium bicarbonate and brine. The solution was dried over anhydrous sodium sulfate, filtered and evaporated in vacuo to yield a solid (8.01 g) which was purified by flash chromatography on silica gel eluting with 20% ethyl acetate in hexane to provide the title compound (6.03 g) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.30 (s, 3H), 5.20 (br, 4H), 6.05 (d, 2H), 6.70 (s, 1H), 6.85 (br, 2H), 7.17 (m, 2H), 7.30 (m, 2H), 7.37 (d, 1H).

Step B. [3-Methyl-4-(pyridin-4-yl)phenyl]-[10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-10-yl]methanone

A suspension of (4-bromo-3-methylphenyl)[10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl]methanone of Step A (1.14g, 2.9 mmol), pyridine-4-boronic acid (0.368 mg, 2.9 mmol) and sodium carbonate (0.760 g, 7.2 mmol) in a mixture of toluene (30 mL), water (10mL), and ethanol (5 mL) was sparged with nitrogen for 15 minutes. To this was added tetrakis(triphenylphosphine)palladium(0) (0.027 g) and the mixture was heated to reflux under a static pressure of nitrogen. After 24 hours additional boronic acid (0.128 mg, 1 mmol) and sodium carbonate (0.116 g) were added and the heating

was continued for 24 hours. Additional catalyst (0.012 g) was added and heating was continued for another 24 hours. The mixture was partitioned between ethyl acetate and hexane. The water layer was washed twice with ethyl acetate and the combined organic layers were dried over anhydrous magnesium sulfate and stripped to a solid. Flash chromatography of the residue on silica gel eluting with 30% ethyl acetate in hexane provided a solid which was recrystallized from ethyl acetate/hexane to provide the title compound (0.254 g) as tan plates m.p. 208-210 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 1.75 (s, 3H), 1.77 (s, 3H), 5.18 (br, 4H), 5.89 (s, 2H), 6.05 (br, 1H), 6.08 (t, 1H), 6.69 (t, 1H), 6.85 (br, 1H), 7.03 (br, 3H), 7.16 (t,1H), 7.35 (d, 1H).

MS [EI, m/z]: 379 $[M]^{+\cdot}$

Anal. Calcd. for $C_{25}H_{21}N_3O$ + 0.5 H_2O: C 77.30, H 5.71, N 10.82.

Found: C 77.01, H 5.37, N 10.68.

Example 32

10-{[3,6-Dimethoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine

Step A. 2,5-Dimethoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-carboxylic acid

A suspension of 4-bromo-2,5-dimethoxybenzoic acid [prepared in the manner of Bortnik et al., *Zh. Org. Khim.* 8, 340 (1972)] (2.43g, 9 mmol), 2-trifluoromethylphenyl boronic acid (5.3 g, 28 mmol), and potassium carbonate (6.21g, 60 mmol) in dioxane (40 mL) was sparged with nitrogen and treated with tetrakis(triphenylphosphine)palladium(0) (0.328 g, 0.2 mmol). The mixture was heated to reflux for 48 hours, cooled, acidified with 1N hydrochloric acid and extracted with ethyl acetate. The extracts were dried over anhydrous magnesium sulfate, filtered and stripped to a solid which was used as such in the next step.

^{1}H NMR (300 MHz,$CDCl_3$): δ 3.90 (s, 3H), 4.05 (s,3H), 7.30 (d, 1H), 7.70 (s, 1H).

Step B. 10-{[3,6-Dimethoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-[10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine

The title compound was prepared in the manner of Example 31, Step A using 2,5-dimethoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-carboxylic acid of Step A (1.63 g, 5

mmol), oxalyl chloride (700 μL, 8 mmol), N,N-dimethylformamide (10μL), 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine (0.93 g, 5 mmol) and Hünig's base (1.78 ml, 10 mmol). Flash chromatography over silica gel using a solvent gradient from 30% ethyl acetate in hexane to 100% ethyl acetate provided the title compound (0.900 g) as a solid. Recrystallization from acetone/hexane yielded white needles, m.p. 210-213 °C.

^{1}H NMR (400 MHz, DMSO-d_6: δ 3.41 (s, 3H), 3.56 (s, 3H), 5.21 (br, 4H), 5.90 (t, 1H), 5.96 (s, 1H), 6.50 (s, 1H), 6.80 (s, 1H), 7.00 (s, 2H), 7.07 (s, 1H), 7.10 (t, 1H), 7.18 (d, 1H), 7.37 (d, 1H), 7.53 (t, 1H), 7.62 (t, 1H), 7.73 (d, 1H).

MS [(+)ESI, m/z]: 493 $[M+H]^+$.

Anal. Calcd. for $C_{28}H_{23}F_3N_2O_3$: C 68.29, H 4.71, N 5.69. Found: C 67.98, H 4.66, N 5.61.

Example 33

{[10-(2-Methoxy)-2'-chloro-[1,1'-biphenyl]-4-yl]carbonyl}-[(2S)-[(2-pyrrolidin-1-yl)methyl]pyrrolidin-1-yl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl-methanone

10-{[2-methoxy-2'-chloro[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepine-3-carboxylic acid (0.230 g, 0.54 mmol) [prepared from trifluoromethanesulfonic acid 4-formyl-2-methoxy-phenyl ester of Example 19, Step A and 2-chlorophenyl boronic acid, in the manner of Example 19, Steps B-E], 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (0.120 g, 0.625 mmol) and 1-hydroxybenzotriazole (0.087 g, 0.625 mmol) were added to a flask containing N,N-dimethylformamide (15 mL). To the homogeneous solution was added (S)-(+)-1-[(2-pyrrolidin-1-yl)methyl]-pyrrolidine (0.100 g, 0.625 mmol) and stirring continued at room temperature overnight. At the end of this time the solution was poured into water and extracted with ethyl acetate. The combined extracts were washed with water, dried and concentrated and the residue was chromatographed on silica gel, eluting with 95:5 chloroform:methanol. The pure fractions were concentrated, and the residue azeotroped and triturated several times with hexane to yield the title product, m.p. 109 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 1.4-1.98 (m, 8H), 3.57 (m,2H), 4.35 (br, 1H), 5.46 (br, 1H), 5.62 (br, 1H), 6.06 (s,1H), 6.40 (s,1H), 6.84-7.49 (m 7H).

MS [(+)APCI, m/z]: 609 $[M+H]^+$.

Example 34

10-[(6-Chloro-3-methoxy-2'-ethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methylpiperidin-4-yl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

Step A. 10-{[6-Chloro-3-methoxy-2'-ethoxy[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid

Prepared by treatment of 10-{[6-chloro-3-methoxy-2'-ethoxy-1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine of Example 17 with trichloroacetyl chloride, followed by basic hydrolysis of the intermediate trichloroacetate ester in the manner of Example 15, Step D.

Step B. 10-[(6-Chloro-3-methoxy-2'-ethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methylpiperidin-4-yl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

Prepared by coupling the 10-{[6-chloro-3-methoxy-2'-ethoxy[1,1'-biphenyl]-4-yl]-carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid of Step A with 1-methyl-4-(methylamino)piperidine (1.25 equiv.) in the manner of Example 16.

Example 35

N-[3-(Dimethylamino)propyl]-N-methyl-10-[(6-chloro-3-methoxy-2'-fluoro[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

Prepared by coupling of the [(6-chloro-3-methoxy-2'-fluoro-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid of Example 18, with 3-(dimethylaminopropyl)-1-methyl amine (1.25 equiv.), in the manner of Example 11.

Example 36

[4-(3-Dimethylaminopropyl)-piperazin-1-yl]-{10-[4-(naphthalen-1-yl)-phenyl]-carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl-methanone

Step A. 10-[4-(Naphthalen-1-yl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepine-3-carboxylic acid

Prepared by treatment of [4-(naphthalen-1-yl)phenyl] [10,11-dihydro-5H-pyrrolo [2,1c] [1,4]benzodiazepin-10-yl]-methanone of Example 23 with trichloroacetyl chloride, followed by basic hydrolysis of the intermediate trichloroacetate ester in the manner of Example 15, Step D.

Step B. [4-(3-Dimethylaminopropyl)-piperazin-1-yl]-{10-[4-(naphthalen-1-yl)-phenyl]-carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c] [1,4]benzodiazepin-3-yl-methanone

The title compound was prepared by coupling the 10-[4-(naphthalen-1-yl)benzoyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid of Step A, with 1-(3-dimethylamino-propyl)-piperazine (1.25 equiv) in the manner of Example 4.

Example 37

(4-Methyl-piperazin-1-yl)-{10-[2-chloro-[4-(naphthalen-1-yl)]phenyl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl-methanone

Step A. 10-{[2-Chloro-4-(naphthalen-1-yl)phenyl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid

Prepared by treatment of [2-chloro-4-(naphthalen-1-yl)-phenyl]-(10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl)-methanone of Example 24 with trichloro-acetyl chloride, followed by basic hydrolysis of the intermediate trichloroacetate ester in the manner of Example 15, Step D.

Step B. (4-Methyl-piperazin-1-yl)-{10-[2-chloro-[4-(naphthalen-1-yl)]phenyl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl-methanone

The title compound was prepared by the coupling the 10-[2-chloro-4-(naphthalen-1-yl)phenyl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid of Step A, with 1-methyl-piperazine (1.25 equiv) in the manner of Example 2.

Example 38

10-{[2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-8-(piperidine-1-carbonyl)-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid-methyl-(1-methyl-piperidin-4-yl)-amide hydrochloride salt

Step A. 10-{[2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-8-carboxylic acid sodium salt

To a stirred solution of methyl 10-{[2-methyl-2'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-8-carboxylate of Example 26 (0.200 g) in ethanol (5 mL) was added 2.5 N sodium hydroxide (4 mL). The reaction mixture was then stirred overnight at room temperature and the solvent removed in vacuo. The residue was acidified with 2 N hydrochloric acid and extracted with diethyl ether. The combined extracts were dried over anhydrous magnesium sulfate and filtered, and the the filtrate evaporated to dryness. The residue was dissolved in anhydrous ethanol and treated with 2.5 N sodium hydroxide (1.0 equiv.). After stirring for 30 minutes at room temperature, the solvent was removed in vacuo to provide the title compound sodium salt as a white solid, m.p. 210 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.85 (s, 3H), 5.20 (br, 3H), 5.90 (s, 2H), 6,80 (t, 1H), 6.90-7.80 (m, 11H).

MS [(+)APCI, m/z]: 491 $[M+H]^+$.

Anal. Calcd. for $C_{28}H_{21}F_3N_2O_3Na + H_2O$: C, 63.27; H, 4.36; N, 5.27.

Found: C, 63.04; H, 4.21; N, 4.99.

Step B. 8-[(Piperidin-1-yl)carbonyl]- {[2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine

Prepared by coupling of 10-{[2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]-carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-8-carboxylic acid of Step A with piperidine, in the manner of Example 2.

Step C. 10-{[2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-8-(piperidine-1-carbonyl)-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid-methyl-(1-methyl-piperidin-4-yl)-amide hydrochloride salt

Prepared by treatment of 8-[(piperidin-1-yl)carbonyl]-{[2-methyl-2'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine of Step B with diphosgene (1.1 equiv.) and triethylamine (1.5 equiv.) followed by 1-methyl-4-(methylamino)piperidine (1.5 equiv.) in the manner of Example 13.

Example 39

[3-Methyl-4-(pyridin-4-yl)-phenyl]-{[(2S)-3-[(2-pyrrolidin-1-yl)methyl]pyrrolidin-1-yl]-carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-10-yl-methanone

Step A. 10-[3-Methyl-4-(4-pyridinyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1c][1,4] benzodiazepine-3-carboxylic acid

To a stirred solution of [3-methyl-4-(pyridin-4-yl)phenyl][10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-10-yl]methanone of Example 31, Step B (5 mmol) and N,N-diisopropylethyl amine (12 mmol) in dichloromethane (200 mL) cooled to 0°C was added dropwise a solution of trichloroacetyl chloride (12 mmol) in dichloromethane. The temperature was maintained at 0°C until the addition was complete. The reaction was stirred overnight as it warmed to room temperature. The solution was then washed with 10% aqueous sodium bicarbonate and the organic layer was dried, concentrated and filtered through a pad of silica gel with 1:1 ethyl acetate/hexane containing 0.1% acetic acid. The filtrate was concentrated in vacuo and the residue was dissolved in acetone and 1N sodium hydroxide (2:1,v/v) and stirred at room temperature for 1 hour and then the pH was adjusted to pH 4 with glacial acetic acid. The solution was concentrated to one half the volume in vacuo and the residue extracted with ethyl acetate. The combined organic layers were dried and evaporated to an oil which was triturated with hexane to yield a solid (0.98 g).

Step B. [3-Methyl-4-(pyridin-4-yl)-phenyl]-{[(2S)-3-[(2-pyrrolidin-1-yl)methyl] pyrrolidin-1-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-10-yl-methanone

The title compound was obtained from the carboxylic acid of Step A and (S)-(+)-1-[(2-pyrrolidinyl)methyl]-pyrrolidine ((1.2 equiv.), in the manner of Example 20.

Example 40

10-[(6-Phenyl-pyridin-3-yl)carbonyl]- N-methyl-N-(1-methyl-piperidin-4-yl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

Step A. 10-(Methoxycarbonyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid

A solution of 10,11-dihydro-5H-pyrrolo[2,1-c][1,4] benzodiazepine (5 mmol) and N,N-diisopropylethyl amine (12 mmol) in dichloromethane (100 mL) was cooled to 0 °C and treated dropwise with trichloroacetylchloride (12 mmol) in dichloromethane (20 mL). The solution was maintained at 0 °C for two hours and then allowed to warm to room temperature overnight. The solution was then treated with methanol (25 mL) and stirring was continued for 2 hours. The solution was washed with 0.1N hydrochloric acid, water and brine, dried over anhydrous magnesium sulfate, filtered and concentrated to yield the title compound as a white solid, m.p. 153-154 °C (dec.).

Anal. Calcd. for $C_{15}H_{14}N_2O_4$ + 0.06 $C_4H_8O_2$ + 0.07 C_3H_6O: C 62.77, H 5.08, N 9.48. Found: C 62.26, H 5.22, N 9.37.

Step B. 10-(Methoxycarbonyl)-[N-methyl-N-(1-methyl-piperidin-4-yl)]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

The title compound was prepared by coupling the 10-(methoxycarbonyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid of step A with 1-methyl-4-(methylamino)piperidine (1.2 equiv.), in the manner of Example 38.

Step C. N-Methyl-N-(1-methyl-piperidin-4-yl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

A solution of 10-(methoxycarbonyl)-[N-methyl-N-(1-methyl-piperidin-4-yl)]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide (5 mmol) of Step B in methanol (50 mL) was treated with potassium carbonate and stirred at room temperature overnight. Water was then added to the solution and the pH adjusted to 6 with 6N hydrochloric acid. The solution was extracted with ethyl acetate, and the combined organic layers were dried over anhydrous magnesium sulfate, and evaporated to dryness The residual oil was triturated with ethyl acetate and hexane to yield the title compound as a powder.

Step D. 10-[(6-Phenyl-pyridin-3-yl)carbonyl]- N-methyl-N-(1-methyl-piperidin-4-yl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

A solution of 6-phenyl-nicotinyl chloride (6 mmol) (prepared by the method of Ogawa et al., WO 9534540) in dichloromethane (20mL) was added dropwise to a cold (0°C) solution of N-Methyl-N-(1-methyl-piperidin-4-yl)-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepine-3-carboxamide of Step C (5 mmol) and N,N-diisopropylethyl amine (6 mmol) in dichloromethane (100 mL). The solution was stirred at 0°C for 2 hours and then allowed to warm to room temperature overnight. The solution was washed with pH 6 buffer, and brine, dried over anhydrous sodium sulfate, filtered and concentrated. The residue was chromatographed on silica gel using 5% methanol in chloroform containing 0.5% ammonium hydroxide, to provide the title compound.

Example 41

[4-(3-Dimethylaminopropyl)-piperazin-1-yl]-[10-[(2'-methoxy-2-methyl-[1,1'-bi-phenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl]-methanone

Prepared by treatment of 10-[(2'-methoxy-2-methyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid of Example 9, with 1-[(3-dimethylamino)propyl]-piperazine (1.2 equiv.) in the manner of Example 4.

Example 42

N-[2-(Dimethylamino)ethyl]-10-{[6-chloro-3-methoxy-2'-(trifluoromethyl)[1,1'-bi-phenyl]-4-yl]carbonyl}-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3 carboxamide

Prepared by treatment of 10-{[6-chloro-3-methoxy-2'-trifluoromethyl-[1,1'-bi-phenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid of Example 15 with 3-(dimethylamino)ethy-1-methylamine (1.2 equiv.), in the manner of Example 22.

Example 43

10-[(2'-Chloro-6-chloro-3-methoxy-[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methylpiperidin-4-yl)-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxamide

To a stirred solution of 10-{[2'-chloro-6-chloro-3-methoxy-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid of Example 16, Step C (0.250 g, 0.49 mmol) was added 1-methyl-4-(methylamino)-piperidine (0.076 g, 0.59 mmol) followed by 1-hydroxybenzotriazole (0.073 g, 0.54 mmol), 1-[3-(dimethylamino)propyl]-3-ethyl carbodiimide hydrochloride (0.093 g, 0.54 mmol), and N,N-diisopropylethyl amine (0.096 g, 0.74 mmol). After stirring overnight, the reaction mixture was diluted with chloroform, washed with saturated aqueous sodium bicarbonate and brine, dried over anhydrous magnesium sulfate, filtered and evaporated to dryness. The residue was flash chromatographed over silica gel eluting with 5% methanol in chloroform containing 0.5% ammonium hydroxide, to provide the title compound as white powder (0.100 g), 92.95% pure by analytical HPLC [Primesphere C-18 column (2.0 x 150 mm); mobile phase: gradient from 10 to 90% acetonitrile/water containing 0.1% phosphoric acid, 2 to 20 minute gradient].

^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.22 (s, 1H), 1.77 (br, 2H), 1.97 (br, 2H), 2.89 (s, 3H), 3.44 (br, 3H), 5.29 (s, 2H), 6.08 (d, 1H), 6.26 (d, 1H), 6.68 (s, 1H), 6.97-7.61 (m, 10H).

MS [(+)ESI, m/z]: 617 $[M+H]^+$.

Anal. Calcd. for $C_{34}H_{34}Cl_2N_4O_3$ + 0.25 $C_4H_8O_2$: C 65.73, H 5.67, N 8.76.

Found: C 65.95, H 5.82, N 8.49.

Example 44

{3-[4-(3-Dimethylamino-propyl)-piperazin-1-yl]carbonyl}-[4-(4-methyl-naphthalen-1-yl)phenyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-10-yl-methanone

Step A. 10-{[4-(4-Methyl-naphthalen-1-yl)phenyl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid

Prepared from [4-(4-methyl-naphthalen-1-yl)-phenyl]-[10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepine-10-yl]methanone of Example 25 by treatment with trichloro-

acetyl chloride, followed by basic hydrolysis of the intermediate trichloroacetate ester in the manner of Example 1, Steps E and F.

Step B. {3-[4-(3-Dimethylamino-propyl)-piperazin-1-yl]carbonyl}-[4-(4-methyl-naphthalen-1-yl)phenyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-10-yl-methanone

Prepared by the coupling of 10-{[4-(4-methyl-naphthalen-1-yl)phenyl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid of Step A, with 1-[3-(dimethylamino)propyl]-piperazine (1.2 equiv.) in the manner of Example 4.

Example 45

10-{[6-(Naphthalen-1-yl)-pyridin-3-yl]carbonyl}-N-methyl-N-(1-methyl-piperidin-4-yl)-10,11-dihydro-5H-pyrrolo[1,2-c][1,4]benzodiazepine-3-carboxamide

Step A. 10-{[6-(Naphthalen-1-yl)-pyridin-3-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[1,2-c]-[1.4]benzodiazepine-3-carboxylic acid

Prepared from [6-(naphthalen-1-yl)-pyridin-3-yl][10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-10-yl]methanone of Example 28 by treatment with trichloroacetyl chloride, followed by basic hydrolysis of the intermediate trichloroacetate ester in the manner of Example 40, Step A.

Step B. 10-{[6-(Naphthalen-1-yl)-pyridin-3-yl]carbonyl}- N-methyl-N-(1-methyl-piperidin-4-yl)-10,11-dihydro-5H-pyrrolo[1,2-c][1,4]benzodiazepine-3-carboxamide

Prepared by the coupling of 10-{[6-(naphthalen-1-yl)-pyridin-3-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[1,2-c][1.4]benzodiazepine-3-carboxylic acid of Step A, and 1-methyl-4-(methylamino)-piperidine (1.25 equiv) in the manner of Example 40, Step B.

Example 46

{[10-(3,6-Dimethoxy)-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-[(2S)-[(2-pyrrolidin-1-yl)methyl]-pyrrolidin-1-yl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepine-3-yl-methanone

Step A. 10-{[3,6-Dimethoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]-carbonyl}-10,11-dihydro-5H-pyrrolo[1,2-c][1,4] benzodiazepine-3-carboxylic acid

Prepared from 10-{[3,6-dimethoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]-carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4]benzodiazepine of Example 32 and trichloroacetyl chloride, followed by basic hydrolysis of the intermediate trichloroacetate ester, in the manner of Example 1, Steps E and F.

Step B. {[10-(3,6-Dimethoxy)-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-[(2S)-[(2-pyrrolidin-1-yl)methyl]-pyrrolidin-1-yl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzo-diazepine-3-yl-methanone

Prepared from 10-[(3,6-dimethoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]-carbon-yl}-10,11-dihydro-5H-pyrrolo[1,2-c][1,4] benzodiazepine-3-carboxylic acid of Step A and (S)-(+)-1-[(2-pyrrolidin-1-yl)methyl]-pyrrolidine (1 equiv.) in the manner of Example 33.

The following examples were prepared according to the General Procedures A-K described below.

General Procedure A

Step A. An appropriately substituted haloaryl carboxylic acid (1.1 mol) was converted to the acid chloride by using oxalyl chloride (1.5 mmol) and a catalytic amount of N,N-dimethylformamide in dichloromethane. Upon consumption of the acid as determined by HPLC analysis, all volatiles were removed in vacuo. The resulting residue was dissolved in dichloromethane and added dropwise to a stirred and cooled (0°C) solution of an appropriately substituted 10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzo-diazepine (1 mmol) and N,N-diisopropylethyl amine (1.2 mmol) in dichloromethane. After 1-16 hours, the mixture was diluted with dichloromethane and washed with 10% aqueous sodium bicarbonate. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated.

Step B. To the residue was added an appropriately substituted boronic acid (1.2 mmol), potassium carbonate (2.5 mmol), tetrabutylammonium bromide (1 mmol), palladium(II) acetate (3% mole) and water/ acetonitrile (1:1.2 mL). The mixture was heated to 70 °C for 1.5 hours, then ethyl acetate was added and the organic phase washed with water. The solution was filtered through a small plug of Celite and concentrated to dryness.

Step C. The residue was dissolved in dichloromethane and N,N-diisopropylethyl amine (2 mmol) was added. The flask was purged with nitrogen and trichloroacetyl chloride was added dropwise to the stirred reaction mixture. After 16 hours, the reaction was quenched by adding aqueous potassium carbonate (100g/ 300 mL) and the organic phase removed. The aqueous layer was extracted with additional dichloromethane and the combined extracts dried over anhydrous sodium sulfate, filtered and concentrated .

Step D. The crude product from Step C was dissolved in tetrahydrofuran (1 mL) and 2N sodium hydroxide (1.5 mL) was added. The mixture was heated (70 °C) for 1.5 hours, 2N hydrochloric acid was added and the product extracted with ethyl acetate. The organic phase was dried, filtered and concentrated. The residue was purified by column chromatography using a gradient of ethyl acetate in hexane contaning 1% glacial acetic acid as the eluant.

Step E. To a stirred solution of a carboxylic acid of Step D above (1.85 mmol) in anhydrous tetrahydrofuran (14 mL) was added 1,1'-carbonyl diimidazole in one portion. The mixture was stirred at room temperature (6-8 hours). The progress of the reaction was monitored by HPLC and when the starting carboxylic acid was consumed, the mixture was worked up to provide the intermediate imidazolide.

Step F. An aliquot of a tetrahydrofuran solution (400 µL, 0.05 mmole) containing the imidazolide of Step E (0.05 mmol) was treated with a 0.25 M solution of an appropriate amine (0.1 mmol). The mixture was heated at 60 °C and the progress of the reaction followed by HPLC. The solvent was removed and the residue dissolved in dichloromethane (1 mL). The organic phase was washed with brine-water (1:1, v/v, 1 mL) and the aqueous layer extracted with additional dichloromethane. The combined extracts were dried and evaporated to dryness and the residue purified by flash chromatography on silica gel. The column (prepacked in 2.5% methanol in dichloromethane contaning 1% triethylamine) was eluted with a solvent gradient from 2.5 to 5% methanol in dichloromethane, to provide desired title compound. The desired title

compounds were either obtained as crystalline solids by exposure to diethyl ether or were further converted into their salts by any of the following procedures.

Step G. Compounds prepared according to Step E that dissolved in diethyl ether were treated with a stoichiometric amount of 1N hydrochloric acid in diethyl ether whereby the hydrochloride salts precipitated out as white solids. Compounds that did not conform to the above category, were dissolved in the minimal amount of tetrahydrofuran, then diluted with diethyl ether. The hydrochloride salts were formed upon addition of 1N hydrochloric acid in diethyl ether with stirring. Compounds that did not immediately precipitate out of solution were stirred for 12-16 hours whereupon a white solid precipitated out.

General Procedure B

To a stirred solution of an appropriately substituted carboxylic acid of General Procedure A, Step D (2 mmol), 1-ethyl-3-(3-dimethylamino-propyl) carbodiimide (0.229 g, 2.2 mmol) and a catalytic amount of 4-(dimethylamino)pyridine in dichloromethane (6 mL) was added the appropriately substituted amine (2.2 mmol) in dichloromethane (2 mL). The reaction was allowed to stir at room temperature for 16 hours, then diluted with dichloromethane. The organic layer was washed with water, saturated aqueous sodium bicarbonate, dried over anhydrous sodium sulfate and evaporated to dryness. The residue was purified by flash chromatography on silica gel (prepacked in dichloromethane containing 2.5% methanol and 1% triethylamine and eluted with a solvent gradient of 2.5 to 5% methanol in dichloromethane) to provide the desired title compound.

General Procedure C

Triphosgene (742 mg, 2.5 mmol) was added to a stirred solution of a carboxylic acid of General Procedure A, Step D (5.0 mmol) in dichloromethane (10 mL). The clear solution was allowed to stir at room temperature (14 hours) after which time the solution turned red. To the reaction mixture was added a solution of the required amine (10.0 mmol) and N,N-diisopropylethyl amine (10.0 mmol) in dichloromethane (5 mL). The mixture was diluted with dichloromethane and washed with water and brine. The organic phase was dried, filtered and concentrated to afford a residue which was purified by flash

chromatography on silica gel. The column (prepacked in 2.5% methanol in dichloromethane contaning 1% triethylamine) was eluted with a solvent gradient from 2.5 to 5% methanol in dichloromethane, to provide the title compound.

General Procedure D

A stirred solution of a carboxylic acid of General Procedure A, Step D (3.54 mmol) and the appropriately substituted amine (3.72 mmol) in N,N-dimethylformamide (10 mL) was cooled to 0 °C. N,N-diisopropylethyl amine (3.89 mmol) was added and the mixture stirred for five minutes. O-(1-Benzotriazolyl)-N, N, N', N'-tetramethyluronium hexafluorophosphate (HBTU) (1.42 g, 3.72 mmol) was added to the mixture in one portion. HPLC analysis revealed that the reaction was complete within five minutes. The solvent was removed at reduced pressure. The residue was diluted with water and extracted with ethyl acetate. The combined extracts were dried and concentrated to dryness. The residue was purified by flash chromatography on silica gel (prepacked in ethyl acetate containing 2% triethylamine and eluted with 100% ethyl acetate) to provide the title compound.

General Procedure E

To a 0.25 M solution of a carboxylic acid of General Procedure A, Step D (200 μL) in N,N-dimethylformamide was added sequentially a 0.5 M solution of N,N-diisopropylethyl amine (200 μL) in N,N-dimethylformamide, and a 0.25 M solution of O-(7-aza-1-benzotriazolyl)-N, N, N', N'-tetramethyluronium hexafluorophosphate (HATU) (210 μL) in N,N-dimethylformamide. The mixture was stirred vigorously at room temperature and then a 0.25 M solution of the appropriately substituted amine (200 μL) in N,N-dimethylformamide was added. Stirring was continued for 24 hours at room temperature, then the mixture was diluted with ethyl acetate, and washed with 1:1 water/ brine. The organic layer was dried and concentrated to dryness. The residue was purified by flash chromatography on silica gel (prepacked in ethyl acetate containing 2% triethylamine and eluted with 100% ethyl acetate) to provide the title compound.

General Procedure F

Step A. To a solution of an appropriately substituted anilino carboxylic acid in methanol was added thionyl chloride. The mixture was heated for 16 hours. The volatiles were removed under reduced pressure and the hydrochloride salt of the carboxylic acid methyl ester was recovered after trituration with methanol/ diethyl ether. The solid was dissolved in concentrated hydrochloric acid and cooled. An aqueous solution of sodium nitrite was added and the mixture was stirred at 0 °C for one hour. An aqueous solution of KI/I_2 was prepared and added to the cooled mixture so that the reaction temperature did not exceed 0 °C. After 1-2 hours the reaction was complete as evidenced by TLC/HPLC analysis. The product was recovered by extraction with ethyl acetate. The combined extracts were dried, filtered and concentrated to afford the desired substituted aryl iodide which could be further purified by recrystallization.

Step B. To a solution of an appropriately substituted aryl halide methyl ester of Step A (2 mmol) and an appropriately substituted boronic acid (2 mmol) in 20% aqueous acetone was added cesium carbonate (3 mmol) followed by palladium(II) acetate (60 μmol). The mixture was heated (70 °C) with stirring for 8-16 hours. The reaction was concentrated to remove the acetone after TLC/HPLC analysis indicated the reaction was complete. The aqueous phase was extracted with ethyl acetate and the combined extracts were filtered through a pad of Celite. The filtrate was washed with 5% aqueous sodium bicarbonate and brine, dried over anhydrous sodium sulfate, filtered and evaporated to dryness. The residue was purified by flash chromatography on silica gel .

Step C. The product from Step B was dissolved in tetrahydrofuran (1 mL) and 2N sodium hydroxide (1.5 mL) was added. The mixture was heated (70 °C) for 1.5 hours, 2N hydrochloric acid was added and the product extracted with ethyl acetate. The organic phase was dried, filtered and concentrated. The residue was purified by column chromatography using ethyl acetate in hexane contaning 1% glacial acetic acid as the eluant.

Step D. To a suspension of the carboxylic acid of Step C (60 μmol) in dichloromethane (100 μL) was added a 0.45 M solution of oxalyl chloride (200 μL) in

dichloromethane followed by dichloromethane (100 μL) containing a catalytic amount of N,N-dimethylformamide. The mixture was allowed to sit at room temperature for 16 hours, then the volatiles were removed in vacuo to afford the crude acid chloride. A solution of the acid chloride in tetrahydrofuran (0.3 M, 200 μL), was utilized to acylate a solution (0.3 M, 200 μL) of an appropriately substituted 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine in tetrahydrofuran according to the General Procedure A, Step A.

General Procedure G

A mixture of an appropriately substituted aryl bromide methyl ester (or an aryl iodide methyl ester of General Procedure F, Step A) (8.3 mmol), an appropriately substituted boronic acid (9.1 mmol), potassium carbonate (20.8 mmol), tetrabutyl-ammonium bromide (or iodide) (8.3 mmol), palladium(II) acetate and water (8-9 mL) was stirred with heating (70 °C) for 1.5 hours, whereupon the reaction was deemed complete by HPLC analysis. The oily upper layer was extracted with ethyl acetate, the extracts washed with brine , dried and concentrated to dryness. The residue was filtered through a column of silica gel to provide the desired coupled product of General Procedure F, Step B.

General Procedure H

The coupling of an appropriately substituted aryl bromide methyl ester (or an aryl iodide methyl ester of General Procedure F, Step A) (8.3 mmol) to an appropriately substituted pyridyl borane was carried out using potassium hydroxide as the base, in the presence of tetrabutylammonium bromide (or iodide) and a tetrakis(triphenylphoshine) palladium (0) catalyst essentially according to the published procedure of M. Ishikura, *Synthesis,* 936-938 (1994), to provide the desired coupled product of General Procedure F, Step B.

General Procedure I

The coupling of an appropriately substituted aryl bromide methyl ester (or an iodide methyl ester of General Procedure F, Step A) (8.3 mmol) to an appropriately

substituted boronic acid was carried out essentially according to General Procedure F, Step B except that the solvent was acetonitrile.

General Procedure J

The desired substituted aryl iodide of General Procedure F, Step A was prepared by reaction of an appropriately substituted amino carboxylic acid in concentrated hydrochloric acid at 0 °C with an aqueous solution of sodium nitrite followed by the addition of an aqueous solution of KI/I_2 at 0 °C, followed by esterification of the resulting iodo aryl carboxylic acid with methanolic hydrochloric acid.

General Procedure K

The acylation of an activated appropriately substituted arylpyridine carboxylic acid of Procedure H was carried out by dissolving the acid (0.06 mmol) in a solution of oxalyl chloride in dichloromethane (12 mg/ 200 μL) followed by a catalytic amount of N,N-dimethylformamide in dichloromethane (100 μL). After stirring at room temperature for 16 hours, the volatiles were removed and tetrahydrofuran added, followed by the addition of a solution of the appropriately substituted 10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine and N,N-diisopropylethyl amine (1:2 molar ratio) in tetrahydrofuran. After stirring for 20 hours, the reaction was worked up essentially as described in General Procedure A, Step A.

Example 47

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 569.23190 $[M+H]^+$. Calcd. for $C_{33}H_{34}ClN_4O_3$: 569.23140

Example 48

{10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 521.25443 $[M+H]^+$. Calcd. for $C_{32}H_{33}N_4O_3$: 521.25472.

Example 49

{10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 535.26907 $[M+H]^+$. Calcd. for $C_{33}H_{35}N_4O_3$: 535.27037

Example 50

{10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 519.27490 $[M+H]^+$. Calcd. for $C_{33}H_{35}N_4O_2$: 519.27546.

Example 51

{10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 535.26968 $[M+H]^+$. Calcd. for $C_{33}H_{35}N_4O_3$: 535.27037

Example 52

{10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 505.25870 $[M+H]^+$. Calcd. for $C_{32}H_{33}N_4O_2$: 505.25981

Example 53

{10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 535.26942 $[M+H]^+$. Calcd for $C_{33}H_{35}N_4O_3$: 535.27037

Example 54

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 585.22598 $[M+H]^+$. Calcd. for $C_{33}H_{34}ClN_4O_4$: 585.22631.

Example 55

{10-[3-M ethoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 571.26974 $[M+H]^+$. Calcd. for $C_{36}H_{35}N_4O_3$: 571.27037.

Example 56

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 551.26482 $[M+H]^+$. Calcd. for $C_{33}H_{35}N_4O_4$: 551.26529

Example 57

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 551.26514 $[M+H]^+$. Calcd. for $C_{33}H_{35}N_4O_4$: 551.26529

Example 58

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 575.22071 $[M+H]^+$. Calcd. for $C_{35}H_{32}ClN_4O_2$: 575.22083

Example 59

(4-Methyl-1,4-diazepan-1-yl)(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]-carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)methanone

HRMS [(+)ESI, m/z]: 587.26266 $[M+H]^+$. Calcd. for $C_{34}H_{34}F_3N_4O_2$: 587.26284

Example 60

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [(+)ESI, m/z]: 583.24744 $[M+H]^+$. Calcd. for $C_{34}H_{36}ClN_4O_3$: 583.24705

Example 61

{10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [(+)ESI, m/z]: 535.26998 $[M+H]^+$. Calcd. for $C_{33}H_{35}N_4O_3$: 535.27037

Example 62

{10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [(+)ESI, m/z]: 549.28533 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_3$: 549.28602

Example 63

{10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [(+)ESI, m/z]: 533.29054 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_2$: 533.29111

Example 64

{10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [(+)ESI, m/z]: 549.28413 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_3$: 549.28602

Example 65

{10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [(+)ESI, m/z]: 519.27474 $[M+H]^+$. Calcd. for $C_{33}H_{35}N_4O_2$: 519.27546

Example 66

{10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [(+)ESI, m/z]: 549.28529 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_3$:. 549.28602

Example 67

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [(+)ESI, m/z]: 599.24153 $[M+H]^+$. Calcd. for $C_{34}H_{36}ClN_4O_4$: 599.24196

Example 68

{10-[3-Methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [ESI(+), m/z]: 585.28342 $[M+H]^+$. Calcd. for $C_{37}H_{37}N_4O_3$: 585.28602

Example 69

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [(+)ESI, m/z]: 565.28058 $[M+H]^+$. Calcd. for $C_{37}H_{37}N_4O_3$: 565.28094

Example 70

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [(+)ESI, m/z]: 565.28111 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_4$: 565.28094

Example 71

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzo-diazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [(+)ESI, m/z]: 589.23633 $[M+H]^+$. Calcd. for $C_{36}H_{34}ClN_4O_2$: 589.23648

Example 72

N-[3-(Dimethylamino)propyl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 537.28687 $[M+H]^+$. Calcd. for $C_{33}H_{37}N_4O_3$: 537.28602

Example 73

N-[3-(Dimethylamino)propyl]-10-[(2,2'-dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 521.29049 $[M+H]^+$. Calcd. for $C_{33}H_{37}N_4O_2$: 521.29111

Example 74

N-[3-(Dimethylamino)propyl]-10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [ESI(+), m/z]: 537.28588 $[M+H]^+$. Calcd. for $C_{33}H_{37}N_4O_3$: 537.28602

Example 75

N-[3-(Dimethylamino)propyl]-10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 523.26977 $[M+H]^+$. Calcd. for $C_{32}H_{35}N_4O_3$: 523.27037

Example 76

N-[3-(Dimethylamino)propyl]-10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 507.27437 $[M+H]^+$. Calcd. for $C_{32}H_{35}N_4O_2$: 507.27546

Example 77

N-[3-(Dimethylamino)propyl]-10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 537.28577 $[M+H]^+$. Calcd. for $C_{33}H_7N_4O_3$: 537.28602

Example 78

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethyl-amino)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 571.24731 $[M+H]^+$. Calcd. for $C_{33}H_{36}ClN_4O_3$: 571.24705

Example 79

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)-propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 587.24161 $[M+H]^+$. Calcd. for $C_{33}H_{36}ClN_4O_4$: 587.24196

Example 80

N-[3-(Dimethylamino)propyl]-10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 573.28422 $[M+H]^+$. Calcd. for $C_{36}H_{37}N_4O_3$: 573.28602

Example 81

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 553.27855 $[M+H]^+$. Calcd. for $C_{33}H_{37}N_4O_4$: 553.28094

Example 82

10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 553.28083 $[M+H]^+$. Calcd. for $C_{33}H_{37}N_4O_4$: 553.28094

Example 83

10-[2-Chloro-4-(1-naphthyl)benzoyl]-N-[3-(dimethylamino)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 577.23637 $[M+H]^+$. Calcd. for $C_{35}H_{34}ClN_4O_2$: 577.23648

Example 84

N-[3-(Dimethylamino)propyl]-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1.4]benzodiazepine-3-carboxamide

HRMS [(+),ESI m/z]: 575.26427 $[M+H]^+$. Calcd. for $C_{33}H_{33}F_3N_4O_2$: 575.26284

Example 85

N-[2-(Dimethylamino)ethyl]-N-methyl-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 575.26180 $[M+H]^+$. Calcd. for $C_{33}H_{34}F_3N_4O_2$: 575.26284

Example 86

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(dimethylamino)ethyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 571.24735 $[M+H]^+$. Calcd. for $C_{33}H_{36}ClN_4O_3$: 571.24705

Example 87

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(dimethylamino)-ethyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 587.24165 $[M+H]^+$. Calcd. for $C_{35}H_{36}ClN_4O_4$: 587.24196

Example 88

N-[2-(Dimethylamino)ethyl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 537.28481 $[M+H]^+$. Calcd. for $C_{33}H_{37}N_4O_3$: 537.28602

Example 89

N-[2-(Dimethylamino)ethyl]-10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 537.28523 $[M+H]^+$. Calcd. for $C_{33}H_{37}N_4O_3$: 537.28602

Example 90

N-[2-(Dimethylamino)ethyl]-10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 523.26992 $[M+H]^+$. Calcd. for $C_{32}H_{35}N_4O_3$: 523.27037

Example 91

N-[2-(Dimethylamino)ethyl]-N-methyl-10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 507.27458 $[M+H]^+$. Calcd. for $C_{32}H_{35}N_4O_2$: 507.27546

Example 92

N-[2-(Dimethylamino)ethyl]-10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 537.28550 $[M+H]^+$. Calcd. for $C_{33}H_{37}N_4O_3$: 537.28602

Example 93

N-[2-(Dimethylamino)ethyl]-10-[3-methoxy-4-(1-naphthyl)benzoyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 573.28467 $[M+H]^+$. Calcd. for $C_{36}H_{37}N_4O_3$: 573.28602

Example 94

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(dimethylamino)ethyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 553.28019 $[M+H]^+$. Calcd. for $C_{33}H_{37}N_4O_4$: 553.28094

Example 95

10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(dimethylamino)ethyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 553.28093 $[M+H]^+$. Calcd. for $C_{33}H_{37}N_4O_4$: 553.28094

Example 96

10-[2-Chloro-4-(1-naphthyl)benzoyl]-N-[2-(dimethylamino)ethyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 577.23624 $[M+H]^+$. Calcd. for $C_{35}H_{34}ClN_4O_2$: 577.23648

Example 97

N-[3-(Dimethylamino)propyl]-N-methyl-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 589.27641 $[M+H]^+$. Calcd. for $C_{34}H_{36}F_3N_4O_2$: 589.27849

Example 98

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)propyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 585.26286 $[M+H]^+$. Calcd. for $C_{34}H_{38}ClN_4O_3$: 585.26270

Example 99

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)-propyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [ESI(+), m/z]: 601.25755 $[M+H]^+$. Calcd. for $C_{34}H_{38}ClN_4O_4$: 601.25761

Example 100

N-[3-(Dimethylamino)propyl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 551.30068 $[M+H]^+$. Calcd. for $C_{34}H_{39}N_4O_3$: 551.30167

Example 101

N-[3-(Dimethylamino)propyl]-10-[(2,2'-dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 535.30614 $[M+H]^+$. Calcd. for $C_{34}H_{39}N_4O_2$: 535.30676

Example 102

N-[3-(Dimethylamino)propyl]-10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 551.30006 $[M+H]^+$. Calcd. for $C_{34}H_{39}N_4O_3$: 551.30167

Example 103

N-[3-(Dimethylamino)propyl]-10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 537.28544 $[M+H]^+$. Calcd. for $C_{33}H_{37}N_4O_3$: 537.28602

Example 104

N-[3-(Dimethylamino)propyl]-N-methyl-10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI m/z]: 521.28955 $[M+H]^+$. Calcd. for $C_{33}H_{37}N_4O_2$: 521.29111

Example 105

N-[3-(Dimethylamino)propyl]-10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 551.30117 $[M+H]^+$. Calcd. for $C_{34}H_{39}N_4O_3$: 551.30167

Example 106

N-[3-(Dimethylamino)propyl]-10-[3-methoxy-4-(1-naphthyl)benzoyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 587.30108 $[M+H]^+$. Calcd. for $C_{37}H_{39}N_4O_3$: 587.30167

Example 107

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)propyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 567.29434 $[M+H]^+$. Calcd. for $C_{34}H_{39}N_4O_4$: 567.29659

Example 108

10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)propyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 567.29641 $[M+H]^+$. Calcd. for $C_{34}H_{39}N_4O_4$: 567.29659

Example 109

10-[2-Chloro-4-(1-naphthyl)benzoyl]-N-[3-(dimethylamino)propyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 591.25210 $[M+H]^+$. Calcd. for $C_{36}H_{36}ClN_4O_2$: 591.25213

Example 110

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl] methanone

HRMS [(+)ESI, m/z]: 637.29447 $[M+H]^+$. Calcd. for $C_{38}H_{42}ClN_4O_3$: 637.29400

Example 111

{10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 589.31729 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_3$: 589.31732

Example 112

{10-[(2-Methyl-2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 603.33228 $[M+H]^+$. Calcd. for $C_{38}H_{43}N_4O_3$: 603.33297

Example 113

{10-[(2-Methyl-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 587.33759 $[M+H]^+$. Calcd. for $C_{38}H_{43}N_4O_2$: 587.33806

Example 114

{10-[(2-Methyl-3'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 603.33180 $[M+H]^+$. Calcd. for $C_{38}H_{43}N_4O_3$: 603.33297

Example 115

{10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 573.32176 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_2$: 573.32241

Example 116

{10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 603.33259 $[M+H]^+$. Calcd. for $C_{38}H_{43}N_4O_3$: 603.33297

Example 117

{10-[(6-Chloro-3-methoxy-3'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 653.28981 $[M+H]^+$. Calcd. for $C_{38}H_{42}ClN_4O_4$: 653.28891

Example 118

{10-[3-Methoxy-4-(1-naphthyl)-benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 639.33115 $[M+H]^+$. Calcd. for $C_{41}H_{43}N_4O_3$: 639.33297

Example 119

{10-[(2,2'-Dimethoxy-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 619.32688 $[M+H]^+$. Calcd. for $C_{38}H_{43}N_4O_4$: 619.32789

Example 120

{10-[(2,3'-Dimethoxy-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 619.32835 $[M+H]^+$. Calcd. for $C_{38}H_{43}N_4O_4$: 619.32789

Example 121

{10-[(2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 643.28413 $[M+H]^+$. Calcd. for $C_{40}H_{40}ClN_4O_2$: 643.28343

Example 122

{10-[(2-Methyl-2'-(trifluoromethyl) -[1,1'-biphenyl]-4-yl)carbonyl]- 10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl] methanone

HRMS [(+)ESI, m/z]: 641.30863 $[M+H]^+$. Calcd. for $C_{38}H_{40}F_3N_4O_2$: 641.30979

Example 123

N-[3-(1H-Imidazol-1-yl)propyl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 560.26553 $[M+H]^+$. Calcd. for $C_{34}H_{34}N_5O_3$: 560.26562

Example 124

10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(1H-imidazol-1-yl)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 544.26958 $[M+H]^+$. Calcd. for $C_{34}H_{34}N_5O_2$: 544.27071

Example 125

N-[3-(1H-Imidazol-1-yl)propyl]-10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 560.26510 $[M+H]^+$. Calcd. for $C_{34}H_{34}N_5O_3$: 560.26562

Example 126

N-[3-(1H-Imidazol-1-yl)propyl]-10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 546.24888 $[M+H]^+$. Calcd. for $C_{33}H_{32}N_5O_3$: 546.24997

Example 127

N-[3-(1H-Imidazol-1-yl)propyl]-10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/]: 530.25497 $[M+H]^+$. Calcd. for $C_{33}H_{32}N_5O_2$: 530.25506

Example 128

N-[3-(1H-Imidazol-1-yl)propyl]-10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 560.26575 $[M+H]^+$. Calcd. for $C_{34}H_{34}N_5O_3$: 560.26562

Example 129

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(1H-imidazol-1-yl)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 594.22579 $[M+H]^+$. Calcd. for $C_{34}H_{33}ClN_5O_3$: 594.22665

Example 130

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(1H-imidazol-1-yl)-propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 610.22084 $[M+H]^+$. Calcd. for $C_{34}H_{32}ClN_5O_4$: 610.22156

Example 131

N-[3-(1H-Imidazol-1-yl)propyl]-10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 596.26527 [$M+H]^+$. Calcd. for $C_{37}H_{34}N_5O_3$: 596.26562

Example 132

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(1H-imidazol-1-yl)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 576.26044 $[M+H]^+$. Calcd. for $C_{34}H_{34}N_5O_4$: 576.26054

Example 133

10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(1H-imidazol-1-yl)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 576.26011 $[M+H]^+$. Calcd. for $C_{34}H_{34}N_5O_4$: 576.26054

Example 134

10-[2-Chloro-4-(1-naphthyl)benzoyl]-N-[3-(1H-imidazol-1-yl)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 600.21491 $[M+H]^+$. Calcd. for $C_{36}H_{31}ClN_5O_2$: 600.21608

Example 135

N-[3-(1H-Imidazol-1-yl)propyl]-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]-carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 598.24213 $[M+H]^+$. Calcd. for $C_{34}H_{31}F_3N_5O_2$: 598.24244

Example 136

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 623.27800 $[M+H]^+$. Calcd. for $C_{37}H_{40}ClN_4O_3$: 623.27835

Example 137

{10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 589.31713 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_3$: 589.31732

Example 138

{10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 573.32179 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_2$: 573.32241

Example 139

{10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 589.31726 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_3$: 589.31732

Example 140

{10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 575.30111 $[M+H]^+$. Calcd. for $C_{36}H_{39}N_4O_3$: 575.30167

Example 141

{10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 559.30724 $[M+H]^+$. Calcd. for $C_{36}H_{39}N_4O_2$: 559.30676

Example 142

{10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 589.31781 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_3$: 589.31732

Example 143

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 639.27294 $[M+H]^+$. Calcd. for $C_{37}H_{40}ClN_4O_4$: 639.27326

Example 144

{10-[3-Methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 625.31794 $[M+H]^+$. Calcd. for $C_{40}H_{41}N_4O_3$: 625.31732

Example 145

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 605.31251 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_4$: 605.31224

Example 146

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z: 605.31137 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_4$: 605.31224

Example 147

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzo-diazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 629.26756 $[M+H]^+$. Calcd. for $C_{39}H_{38}ClN_4O_2$: 629.26778

Example 148

(10-{[2-Methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z]: 627.29365 $[M+H]^+$. Calcd. for $C_{37}H_{38}F_3N_4O_2$: 627.29414

Example 149

10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 563.30179 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_3$: 563.30167

Example 150

10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+) ESI, m/z]: 547.30585 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_2$: 547.30676

Example 151

10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 563.30189 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_3$: 563.30167

Example 152

10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 549.28510 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_3$: 549.28602

Example 153

10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 533.29111 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_2$: 533.29111

Example 154

10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 563.30195 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_3$: 563.30167

Example 155

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 597.26203 $[M+H]^+$. Calcd. for $C_{35}H_{38}ClN_4O_3$: 597.26270

Example 156

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 613.25706 $[M+H]^+$. Calcd. for $C_{35}H_{38}ClN_4O_4$: 613.25761

Example 157

10-[3-Methoxy-4-(1-naphthyl)benzoyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 599.30190 $[M+H]^+$. Calcd. for $C_{38}H_{39}N_4O_3$: 599.30167

Example 158

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 579.29668 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_4$: 579.29659

Example 159

10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 579.29558 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_4$: 579.29659

Example 160

10-[2-Chloro-4-(1-naphthyl)benzoyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 603.25172 $[M+H]^+$. Calcd. for $C_{37}H_{36}ClN_4O_2$: 603.25213

Example 161

10-{[2-Methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-N-[2-(1-piperidinyl)-ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 601.27838 $[M+H]^+$. Calcd. for $C_{35}H_{36}F_3N_4O_2$: 601.27849

Example 162

10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidin-yl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 563.30191 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_3$: 563.30167

Example 163

10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 547.30573 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_2$: 547.30676

Example 164

10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 563.30176 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_3$: 563.30167

Example 165

10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 549.28483 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_3$: 549.28602

Example 166

10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 533.29125 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_2$: 533.29111

Example 167

10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 563.30226 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_3$: 563.30167

Example 168

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 597.26179 $[M+H]^+$. Calcd. for $C_{35}H_{38}ClN_4O_3$: 597.26270

Example 169

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 613.25723 $[M+H]^+$. Calcd. for $C_{35}H_{38}ClN_4O_4$: 613.25761

Example 170

10-[3-Methoxy-4-(1-naphthyl)benzoyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 599.30196 $[M+H]^+$. Calcd. for $C_{38}H_{39}N_4O_3$: 599.30167

Example 171

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 579.29682 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_4$: 579.29659

Example 172

10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)-ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 579.29546 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_4$: 579.29659

Example 173

10-[2-Chloro-4-(1-naphthyl)benzoyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 603.25172 $[M+H]^+$. Calcd. for $C_{37}H_{36}ClN_4O_2$: 603.25213

Example 174

N-[2-(1-Methyl-2-pyrrolidinyl)ethyl]-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 601.27811 $[M+H]^+$. Calcd. for $C_{35}H_{36}F_3N_4O_2$: 601.27849

Example 175

10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 563.30205 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_3$: 563.30167

Example 176

10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 563.30249 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_3$: 563.30167

Example 177

10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 549.28510 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_3$: 549.28602

Example 178

N-Methyl-10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 533.29178 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_2$: 533.29111

Example 179

10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 563.30250 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_3$: 563.30167

Example 180

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 597.26325 $[M+H]^+$. Calcd. for $C_{35}H_{38}ClN_4O_3$: 597.26270

Example 181

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 613.25636 $[M+H]^+$. Calcd. for $C_{35}H_{38}ClN_4O_4$: 613.25761

Example 182

10-[3-Methoxy-4-(1-naphthyl)benzoyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 599.30260 $[M+H]^+$. Calcd. for $C_{38}H_{39}N_4O_3$: 599.30167

Example 183

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 579.29711 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_4$: 579.29659

Example 184

N-Methyl-N-(1-methyl-4-piperidinyl)-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 601.27917 $[M+H]^+$. Calcd. for $C_{35}H_{36}F_3N_4O_2$: 601.27849

Example 185

10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 549.28649 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_3$: 549.28602

Example 186

10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 549.28621 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_3$: 549.28602

Example 187

10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 535.26930 $[M+H]^+$. Calcd. for $C_{33}H_{35}N_4O_3$: 535.27037

Example 188

N-Methyl-10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 519.27588 $[M+H]^+$. Calcd. for $C_{33}H_{35}N_4O_2$: 519.27546

Example 189

10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 549.28615 $[M+H]^+$. Calcd. for $C_{34}H_7N_4O_3$: 549.28602

Example 190

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 583.24598 $[M+H]^+$. Calcd. for $C_{34}H_{36}ClN_4O_3$: 583.24705

Example 191

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 599.24156 $[M+H]^+$. Calcd. for $C_{34}H_{36}ClN_4O_4$: 599.24196

Example 192

10-[3-Methoxy-4-(1-naphthyl)benzoyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 585.28612 $[M+H]^+$. Calcd. for $C_{37}H_{37}N_4O_3$: 585.28602

Example 193

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 565.28108 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_4$: 565.28094

Example 194

N-Methyl-N-(1-methyl-3-pyrrolidinyl)-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [ESI(+), m/z]: 587.26289 $[M+H]^+$. Calcd. for $C_{34}H_{34}F_3N_4O_2$: 587.26284

Example 195

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 592.32843 $[M+H]^+$. Calcd. for $C_{36}H_{42}N_5O_3$: 592.32822

Example 196

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)methanone

HRMS [(+)ESI, m/z]: 630.30472 $[M+H]^+$. Calcd. for $C_{36}H_{39}F_3N_5O_2$: 630.30504

Example 197

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(dimethylamino)ethyl]-1-piperazinyl}-methanone

HRMS [(+)ESI, m/z]: 626.28869 $[M+H]^+$. Calcd. for $C_{36}H_{41}ClN_5O_3$: 626.28925

Example 198

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[(2,2'-dimethyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 576.33266 $[M+H]^+$. Calcd. for $C_{36}H_{42}N_5O_2$: 576.33331

Example 199

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 592.32832 $[M+H]^+$. Calcd. for $C_{36}H_{42}N_5O_3$: 592.32822

Example 200

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[(2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 562.31789 $[M+H]^+$. Calcd. for $C_{35}H_{40}N_5O_2$: 562.31766

Example 201

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 592.32869 $[M+H]^+$. Calcd. for $C_{36}H_{42}N_5O_3$: 592.32822

Example 202

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(dimethylamino)ethyl]-1-piperazinyl}-methanone

HRMS [(+)ESI, m/z]: 642.28388 $[M+H]^+$. Calcd. for $C_{36}H_{41}ClN_5O_4$: 642.28416

Example 203

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 628.32892 $[M+H]^+$. Calcd. for $C_{39}H_{42}N_5O_3$: 628.32822

Example 204

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}{4-[2-(dimethylamino)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 608.32361 $[M+H]^+$. Calcd. for $C_{36}H_{42}N_5O_4$: 608.32314

Example 205

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(dimethylamino)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 632.27795 $[M+H]^+$. Calcd. for $C_{38}H_{39}ClN_5O_2$: 632.27868

Example 206

{10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 634.33902 $[M+H]^+$. Calcd. for $C_{38}H_{44}N_5O_4$: 634.33879

Example 207

{10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 620.32261 $[M+H]^+$. Calcd. for $C_{37}H_{42}N_5O_4$: 620.32314

Example 208

{10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 634.33860 $[M+H]^+$. Calcd. for $C_{38}H_{44}N_5O_4$: 634.33879

Example 209

{10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 604.32832 $[M+H]^+$. Calcd. for $C_{37}H_{42}N_5O_3$: 604.32822

Example 210

{10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 634.33915 $[M+H]^+$. Calcd. for $C_{38}H_{44}N_5O_4$: 634.33879

Example 211

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 650.33299 $[M+H]^+$. Calcd. for $C_{38}H_{44}N_5O_5$: 650.33370

Example 212

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}-methanone

HRMS [(+)ESI, m/z]: 684.29459 $[M+H]^+$. Calcd. for $C_{38}H_{43}ClN_5O_5$: 684.29473

Example 213

{10-[3-Methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 670.33934 $[M+H]^+$. Calcd. for $C_{41}H_{44}N_5O_4$: 670.33879

Example 214

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 650.33399 $[M+H]^+$. Calcd. for $C_{38}H_{44}N_5O_5$: 650.33370

Example 215

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 674.28820 $[M+H]^+$. Calcd. for $C_{40}H_{41}ClN_5O_3$: 674.28925

Example 216

(10-{[2-Methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl){4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}-methanone

HRMS [(+)ESI, m/z]: 672.31528 $[M+H]^+$. Calcd. for $C_{38}H_{41}F_3N_5O_3$: 672.31560

Example 217

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}-methanone

HRMS [(+)ESI, m/z]: 668.29857 $[M+H]^+$. Calcd. for $C_{38}H_{43}ClN_5O_4$: 668.29981

Example 218

{10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 618.34297 $[M+H]^+$. Calcd. for $C_{38}H_{44}N_5O_3$: 618.34387

Example 219

(4-Allyl-1-piperazinyl){10-[(6-chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 595.24716 $[M+H]^+$. Calcd. for $C_{35}H_{36}ClN_4O_3$: 595.24705

Example 220

(4-Allyl-1-piperazinyl){10-[(2,2'-dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 545.29099 $[M+H]^+$. Calcd. for $C_{35}H_{37}N_4O_2$: 545.29111

Example 221

(4-Allyl-1-piperazinyl){10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 547.27057 $[M+H]^+$. Calcd. for $C_{34}H_{35}N_4O_3$: 547.27037

Example 222

(4-Allyl-1-piperazinyl){10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 561.28578 $[M+H]^+$. Calcd. for $C_{35}H_{37}N_4O_3$: 561.28602

Example 223

(4-Allyl-1-piperazinyl){10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 561.28603 $[M+H]^+$. Calcd. for $C_{35}H_{37}N_4O_3$: 561.28602

Example 224

(4-Allyl-1-piperazinyl){10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 531.27586 $[M+H]^+$. Calcd. for $C_{34}H_{35}N_4O_2$: 531.27546

Example 225

(4-Allyl-1-piperazinyl){10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 561.28574 $[M+H]^+$. Calcd. for $C_{35}H_{37}N_4O_3$: 561.28602

Example 226

(4-Allyl-1-piperazinyl){10-[(6-chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 611.24297 $[M+H]^+$. Calcd. for $C_{35}H_{38}ClN_4O_4$: 611.24196

Example 227

(4-Allyl-1-piperazinyl){10-[(2,2'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 577.28073 $[M+H]^+$. Calcd. for $C_{35}H_{37}N_4O_4$: 577.28094

Example 228

(4-Allyl-1-piperazinyl){10-[(2,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 577.28057 $[M+H]^+$. Calcd. for $C_{35}H_{37}N_4O_4$: 577.28094

Example 229

(4-Allyl-1-piperazinyl){10-[2-chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 601.23590 $[M+H]^+$. Calcd. for $C_{37}H_{34}ClN_4O_2$: 601.23648

Example 230

(4-Allyl-1-piperazinyl)(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)methanone

HRMS [(+)ESI, m/z]: 599.26246 $[M+H]^+$. Calcd. for $C_{35}H_{34}F_3N_4O_2$: 599.26284

Example 231

(4-Allyl-1-piperazinyl){10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 597.28585 $[M+H]^+$. Calcd. for $C_{38}H_{37}N_4O_3$: 597.28602

Example 232

(4-Isopropyl-1-piperazinyl){10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 563.30161 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_3$: 563.30167

Example 233

{10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 547.30657 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_2$: 547.30676

Example 234

(4-Isopropyl-1-piperazinyl){10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 549.28582 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_3$: 549.28602

Example 235

(4-Isopropyl-1-piperazinyl){10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 563.30191 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_3$: 563.30167

Example 236

(4-Isopropyl-1-piperazinyl){10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 599.30222 $[M+H]^+$. Calcd. for $C_{38}H_{39}N_4O_3$: 599.30167

Example 237

(4-Isopropyl-1-piperazinyl){10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 563.30167 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_3$: 563.30167

Example 238

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 597.26324 $[M+H]^+$. Calcd. for $C_{35}H_{38}ClN_4O_3$: 597.26270

Example 239

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 613.25831 $[M+H]^+$. Calcd. for $C_{35}H_{38}ClN_4O_4$: 613.25761

Example 240

(4-Isopropyl-1-piperazinyl)(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)methanone

HRMS [(+)ESI, m/z]: 601.27873 $[M+H]^+$. Calcd. for $C_{35}H_{36}F_3N_4O_2$: 601.27849

Example 241

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 579.29699 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_4$: 579.29659

Example 242

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 579.29628 $[M+H]^+$. Calcd. for $C_{35}H_{39}N_4O_4$: 579.29659

Example 243

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 603.25170 $[M+H]^+$. Calcd. for $C_{37}H_{36}ClN_4O_2$: 603.25213

Example 244

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 533.29134 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_2$: 533.29111

Example 245

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}-methanone

HRMS [(+)ESI, m/z]: 606.34402 $[M+H]^+$. Calcd. for $C_{37}H_{44}N_5O_3$: 606.34387

Example 246

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[(2'-methoxy[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 592.32795 $[M+H]^+$. Calcd. for $C_{36}H_{42}N_5O_3$: 592.32822

Example 247

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[(2,2'-dimethyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 590.34875 $[M+H]^+$. Calcd. for $C_{37}H_{44}N_5O_2$: 590.34896

Example 248

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}-methanone

HRMS [(+)ESI, m/z]: 606.34364 $[M+H]^+$. Calcd. for $C_{37}H_{44}N_5O_3$: 606.34387

Example 249

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 576.33344 $[M+H]^+$. Calcd. for $C_{36}H_{42}N_5O_2$: 576.33331

Example 250

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}-methanone

HRMS [(+)ESI, m/z]: 606.34409 $[M+H]^+$. Calcd. for $C_{37}H_{44}N_5O_3$: 606.34387

Example 251

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[3-(dimethylamino)propyl]-1-piperazinyl}-methanone

HRMS [(+)ESI, m/z]: 640.30437 $[M+H]^+$. Calcd. for $C_{37}H_{43}ClN_5O_3$: 640.30490

Example 252

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[3-(dimethylamino)propyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 656.29921 $[M+H]^+$. Calcd. for $C_{37}H_{43}ClN_5O_4$: 656.29981

Example 253

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 642.34363 $[M+H]^+$. Calcd. for $C_{40}H_{44}N_5O_3$: 642.34387

Example 254

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}{4-[3-(dimethylamino)propyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 622.33914 $[M+H]^+$. Calcd. for $C_{37}H_{44}N_5O_4$: 622.33879

Example 255

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}{4-[3-(dimethylamino)propyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 622.33845 $[M+H]^+$. Calcd. for $C_{37}H_{44}N_5O_4$: 622.33879

Example 256

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzo-diazepin-3-yl}{4-[3-(dimethylamino)propyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 646.29385 $[M+H]^+$. Calcd. for $C_{39}H_{41}ClN_5O_2$: 646.29433

Example 257

{10-[(2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[3-(dimethylamino)propyl]-1-piperazinyl}-methanone

HRMS [ESI(+), m/z: 644.32017 $[M+H]^+$. Calcd. for $C_{37}H_{41}F_3N_5O_2$: 644.32069

Example 258

(10-{[2-Methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]-methanone

HRMS [(+)ESI, m/z]: 627.29381 $[M+H]^+$. Calcd. for $C_{37}H_{38}F_3N_4O_2$: 627.29414

Example 259

{10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 589.31760 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_3$: 589.31732

Example 260

{10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 573.32214 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_2$: 573.32241

Example 261

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzo-diazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 629.26794 $[M+H]^+$. Calcd. for $C_{39}H_{38}ClN_4O_2$: 629.26778

Example 262

{10-[3-Methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzo-diazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 625.31761 $[M+H]^+$. Calcd. for $C_{40}H_{41}N_4O_3$: 625.31732

Example 263

{10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 589.31770 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_3$: 589.31732

Example 264

{10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 559.30704 $[M+H]^+$. Calcd. for $C_{36}H_{39}N_4O_2$: 559.30676

Example 265

{10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 575.30152 $[M+H]^+$. Calcd. for $C_{36}H_{39}N_4O_3$: 575.30167

Example 266

{10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 589.31773 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_3$: 589.31732

Example 267

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]-methanone

HRMS [(+)ESI, m/z]: 623.27896 $[M+H]^+$. Calcd. for $C_{37}H_{40}ClN_4O_3$: 623.27835

Example 268

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]-methanone

HRMS [(+)ESI, m/z]: 639.27238 $[M+H]^+$. Calcd. for $C_{37}H_{40}ClN_4O_4$: 639.27326

Example 269

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 605.31257 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_4$: 605.31224

Example 270

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 605.31209 $[M+H]^+$. Calcd. for $C_{37}H_{41}N_4O_4$: 605.31224

Example 271

[(3R)-3-(Dimethylamino)pyrrolidinyl](10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)-methanone

HRMS [(+)ESI, m/z]: 587.26200 $[M+H]^+$. Calcd. for $C_{34}H_{34}F_3N_4O_2$: 587.26284

Example 272

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 549.28581 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_3$: 549.28602

Example 273

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[(3R)-3-(dimethylamino)pyrrolidinyl]-methanone

HRMS [(+)ESI, m/z]: 583.24837 $[M+H]^+$. Calcd. for $C_{34}H_{36}ClN_4O_3$: 583.24705

Example 274

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[(2,2'-dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 533.29105 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_2$: 533.29111

Example 275

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[(3R)-3-(dimethylamino)pyrrolidinyl]-methanone

HRMS [(+)ESI, m/z]: 599.24184 $[M+H]^+$. Calcd. for $C_{34}H_{36}ClN_4O_4$: 599.24196

Example 276

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 585.28535 $[M+H]^+$. Calcd. for $C_{37}H_{37}N_4O_3$: 585.28602

Example 277

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[(3R)-3-(dimethylamino)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 589.23703 $[M+H]^+$. Calcd. for $C_{36}H_{34}ClN_4O_2$: 589.23648

Example 278

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 549.28594 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_3$: 549.28602

Example 279

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 535.27042 $[M+H]^+$. Calcd. for $C_{33}H_{35}N_4O_3$: 535.27037

Example 280

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 519.27502 $[M+H]^+$. Calcd. for $C_{33}H_{35}N_4O_2$: 519.27546

Example 281

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 549.28607 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_3$: 549.28602

Example 282

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[(3R)-3-(dimethylamino)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 565.28071 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_4$: 565.28094

Example 283

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[(3R)-3-(dimethylamino)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 565.28058 $[M+H]^+$. Calcd. for $C_{34}H_{37}N_4O_4$: 565.28094

Example 284

N-[(1S)-2-Amino-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-10-{[2-methyl-2'-(trifluoro-methyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzo-diazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 627.23303 $[M+H]^+$. Calcd. for $C_{34}H_{30}F_3N_6O_3$: 627.23260

Example 285

N-[(1S)-2-Amino-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-10-[(2'-methoxy[1,1'-bi-phenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 575.23897 $[M+H]^+$. Calcd. for $C_{33}H_{31}N_6O_4$: 575.24013

Example 286

N-[(1S)-2-Amino-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-10-[(2,2'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 605.24974 $[M+H]^+$. Calcd. for $C_{34}H_{33}N_6O_5$: 605.25070

Example 287

N-[(1S)-2-Amino-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-10-[(6-chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzo-diazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 639.21102 $[M+H]^+$. Calcd. for $C_{34}H_{32}ClN_6O_5$: 639.21173

Example 288

N-[(1S)-2-Amino-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-10-[(2'-methoxy-2-methyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 589.25637 $[M+H]^+$. Calcd. for $C_{34}H_{33}N_6O_4$: 589.25578

Example 289

1H-Imidazol-1-yl{10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 503.20731 $[M+H]^+$. Calcd. for $C_{31}H_{27}N_4O_3$: 503.20777

Example 290

1H-Imidazol-1-yl{10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 503.20834 $[M+H]^+$. Calcd. for $C_{31}H_{27}N_4O_3$: 503.20777

Example 291

1H-Imidazol-1-yl{10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 539.20754 $[M+H]^+$. Calcd. for $C_{34}H_{27}N_4O_3$: 539.20777

Example 292

1H-Imidazol-1-yl{10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 503.20760 $[M+H]^+$. Calcd. for $C_{31}H_{27}N_4O_3$: 503.20777

Example 293

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(1H-imidazol-1-yl)methanone

HRMS [(+)ESI, m/z]: 519.20285 $[M+H]^+$. Calcd. for $C_{31}H_{27}N_4O_4$: 519.20269

Example 294

1H-Imidazol-1-yl(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)methanone

HRMS [(+)ESI, m/z]: 541.18438 $[M+H]^+$. Calcd. for $C_{31}H_{24}F_3N_4O_2$: 541.18459

Example 295

N-[(3S)-1-Azabicyclo[2.2.2]oct-3-yl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 561.28517 $[M+H]^+$. Calcd. for $C_{35}H_{37}N_4O_3$: 561.28602

Example 296

N-[(3R)-1-Azabicyclo[2.2.2]oct-3-yl]-10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 547.26933 $[M+H]^+$. Calcd. for $C_{34}H_{35}N_4O_3$: 547.27037

Example 297

N-[(3S)-1-Azabicyclo[2.2.2]oct-3-yl]-10-[(6-chloro-3-methoxy-2'-methyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 595.24661 $[M+H]^+$. Calcd. for $C_{35}H_{36}ClN_4O_3$: 595.24705

Example 298

N-[(3R)-1-Azabicyclo[2.2.2]oct-3-yl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 561.28489 $[M+H]^+$. Calcd. for $C_{35}H_{37}N_4O_3$: 561.28602

Example 299

N-[(3R)-1-Azabicyclo[2.2.2]oct-3-yl]-10-[(2,2'-dimethoxy[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 577.28113 $[M+H]^+$. Calcd. for $C_{35}H_{37}N_4O_4$: 577.28094

Example 300

N-[(3S)-1-Azabicyclo[2.2.2]oct-3-yl]-10-[(2,2'-dimethoxy[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 577.28101 $[M+H]^+$. Calcd. for $C_{35}H_{37}N_4O_4$: 577.28094

Example 301

N-[(3R)-1-Azabicyclo[2.2.2]oct-3-yl]-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 599.26211 $[M+H]^+$. Calcd. for $C_{35}H_{34}F_3N_4O_2$: 599.26284

Example 302

tert-Butyl (5S)-6-amino-5-[({10-[(6-chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}carbonyl)amino]-6-oxohexylcarbamate

HRMS [(+)ESI, m/z]: 730.29945 $[M+H]^+$. Calcd. for $C_{39}H_{45}ClN_5O_7$: 730.30021

Example 303

tert-Butyl (5S)-6-amino-5-[({10-[(2,2'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}carbonyl)amino]-6-oxohexylcarbamate

HRMS [(+)ESI, m/z]: 696.33935 $[M+H]^+$. Calcd. for $C_{39}H_{46}N_5O_7$: 696.33918

Example 304

tert-Butyl (5S)-6-amino-5-[({10-[(6-chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}carbonyl)amino]-6-oxohexylcarbamate

HRMS [(+)ESI, m/z]: 714.30505 $[M+H]^+$. Calcd. for $C_{39}H_{45}ClN_5O_6$: 714.30529

Example 305

{10-(3-Methoxy-4-pyridin-3-yl-benzoyl)-10,11-dihydro-5H-pyrrolo[1,2-c][1,4]benzodiazepin-3-yl}-[4-(1-piperidinyl)-1-piperidinyl]-methanone

MS [(+)ESI, m/z]: 590 $[M+H]^+$. Calcd. for $C_{36}H_{40}N_5O_3$: 590.313

The following examples were prepared according to the General Procedure L described below.

General Procedure L

Step A. To a stirred cooled (0 °C) solution of an appropriately substituted 10-(4-amino)benzoyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine (10 mmol) in dichloromethane (20 mL) was added N,N-diisopropylethyl amine (2.09 mL, 12 mmol) followed by the addition of 9-fluorenylmethyl chloroformate (2.85 g, 11 mmol) in one portion. The reaction was allowed to warm to room temperature. TLC analysis was used to monitor the progress of the reaction and after 8 hours, indicated that a single product was formed. The reaction mixture was diluted with dichloromethane and washed with water and brine. The organic phase was dried over anhydrous sodium sulfate, filtered and concentrated. The resulting residue was purified by flash column chromatography (Biotage Flash 40S, gradient elution from 10 to 20% ethyl acetate in hexanes) to provide the desired appropriately substituted 4-(fluorenylmethoxycarbonyl)-10,11-dihydro-5H-pyrrolo [2,1-c][1,4]benzodiazepine.

Step B. Trichloroacetyl chloride (3.35 mL, 30 mmol) was added to a solution of an appropriately substituted 4-(fluorenylmethoxycarbonyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine of Step A (10 mmol) and N,N-diisopropylethyl amine (3.48 mL, 20 mmol) in dichloromethane, and the solution was stirred at ambient temperature for 2 hours. An aqueous solution of sodium bicarbonate (0.5 M) was added to the mixture and the organic layer was separated, dried over anhydrous sodium sulfate, filtered and concentrated. The residue was dissolved in a solution of piperidine in N,N-dimethyl formamide (20%, v/v) and stirred until the starting material was no longer observed by HPLC/TLC analysis. The mixture was diluted with ethyl acetate and washed with water. The organic phase was dried over anhydrous sodium sulfate, filtered and concentrated. The desired appropriately substituted 2,2,2-trichloro-1-[10-(4-aminobenzoyl)-10,11-dihydro-5H-pyrrolo [2,1-c][1,4]benzodiazepin-3-yl}-ethanone was isolated by flash chromatography (Biotage, Flash 40M, gradient elution from 20 to 30% ethyl acetate in hexanes).

Step C. An appropriately substituted 1,4-diketone (25 mmol) was added to a vial containing an appropriately substituted aniline of Step B (4.4 mmol) followed by the addition of acetic acid (1 mL). The contents of the vial were stirred and heated (80 °C) without the vial capped (to allow for the removal of water). After 1 hour the solution was diluted with ethyl acetate (20 mL). The organic phase was washed with water, aqueous sodium bicarbonate and brine. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated. The resulting residue was purified by flash column chromatography to afford the desired appropriately substituted 2,2,2-trichloro-1-{10-{4-(1H-pyrrol-1-yl)-benzoyl]-10,11-dihydro[2,1-c][1,4]benzodiazepin-3-yl}-ethanone.

Step D. The material from Step C (3.85 mmol) was dissolved in tetrahydrofuran (10 mL) and treated with aqueous sodium hydroxide (2 N, 3 mL). The mixture was allowed to stir with heating (80 °C) overnight. After cooling to room temperature, aqueous hydrochloric acid (2 N, 3.2 mL) was added and product was recovered by extraction with ethyl acetate. The combined extracts were evaporated and the residue purified by flash column chromatography, eluting with a gradient of 20 to 50% ethyl acetate in hexanes to provide the desired appropriately substituted title compound.

Example 306

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 538.28136 $[M+H]^+$. Calcd. for $C_{32}H_{36}N_5O_3$: 538.28127

Example 307

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone

HRMS [(+)ESI, m/z]: 552.29613 $[M+H]^+$. Calcd. for $C_{33}H_{38}N_5O_3$: 552.29692

Example 308

N-[3-(Dimethylamino)propyl]-10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxy-benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 540.29503 $[M+H]^+$. Calcd. for $C_{32}H_{38}N_5O_3$: 540.29692

Example 309

N-[2-(Dimethylamino)ethyl]-10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 540.29642 $[M+H]^+$. Calcd. for $C_{32}H_{38}N_5O_3$: 540.29692

Example 310

N-[3-(Dimethylamino)propyl]-10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 554.31172 $[M+H]^+$. Calcd. for $C_{33}H_{40}N_5O_3$: 554.31257

Example 311

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxy-benzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]-methanone

HRMS [(+)ESI, m/z]: 606.34354 $[M+H]^+$. Calcd. for $C_{37}H_{44}N_5O_3$: 606.34387

Example 312

10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-N-[3-(1H-imidazol-1-yl)-propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 563.27492 $[M+H]^+$. Calcd. for $C_{33}H_{35}N_6O_3$: 563.27652

Example 313

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone

HRMS [(+)ESI, m/z: 592.32816 $[M+H]^+$. Calcd. for $C_{36}H_{42}N_5O_3$: 592.32822

Example 314

10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z]: 566.31192 $[M+H]^+$. Calcd. for $C_{34}H_{40}N_5O_3$: 566.31257

Example 315

10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide

HRMS [(+)ESI, m/z: 566.31226 $[M+H]^+$. Calcd. for $C_{34}H_{40}N_5O_3$: 566.31257

Example 316

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}-methanone

HRMS [(+)ESI, m/z]: 595.33898 $[M+H]^+$. Calcd. for $C_{35}H_{43}N_6O_3$: 595.33912

Example 317

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone

HRMS [(+)ESI, m/z]: 637.34914 $[M+H]^+$. Calcd. for $C_{37}H_{45}N_6O_4$: 637.34968

Example 318

(4-Allyl-1-piperazinyl){10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 564.29788 $[M+H]^+$. Calcd. for $C_{34}H_{38}N_5O_3$: 564.29692

Example 319

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone

HRMS [(+)ESI, m/z]: 566.31184 $[M+H]^+$. Calcd. for $C_{34}H_{40}N_4O_3$: 566.31257

Example 320

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}-methanone

HRMS [(+)ESI, m/z]: 609.35380 $[M+H]^+$. Calcd. for $C_{36}H_{45}N_6O_3$: 609.35477

Example 321

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone

HRMS [(+)ESI, m/z]: 592.32768 $[M+H]^+$. Calcd. for $C_{36}H_{42}N_5O_3$: 592.32822

Example 322

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxy-benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone

HRMS [(+)ESI, m/z]: 552.29598 $[M+H]^+$. Calcd. for $C_{33}H_{38}N_5O_3$: 552.29692

Example 323

[3-(4-Methyl-piperazine-1-carbonyl)-4H-10H-3a, 5, 9-triaza-benzo[f]azulen-9-yl]-(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)-methanone

Step A. 2-Chloromethyl-pyridine-3-carboxylic acid methyl ester

A solution of methyl 2-methylnicotinate (20.0 g, 0.132 mol) and trichloroisocyanuric acid (46.0 g, 0.198 mol) in dichloromethane (100 mL) was stirred at room temperature overnight. The reaction mixture was then washed with saturated aqueous sodium carbonate and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered, and the solvent evaporated in vacuo to provide the title compound as a yellow liquid (11. 2 g), which is used as such in the next step.

Step B. 2-(2-Formyl-pyrrol-1-ylmethyl)-pyridine-3-carboxylic acid methyl ester

To a suspension of sodium hydride (5.8 g, 0.12 mol) in dry N,N-dimethyl formamide (25 mL) was added slowly under nitrogen a solution of pyrrole 2-carboxaldehyde (10.5 g, 0.11 mol) in N,N-dimethylformamide (10 mL), and the reaction mixture was stirred at room temperature for 30 minutes. The reaction was then cooled to 5°C and 2-chloromethyl-pyridine-3-carboxylic acid methyl ester of Step A was added slowly, the temperature being maintained at or below 20 °C. After the addition was complete, the reaction was stirred at room temperature for 30 minutes. The mixture was evaporated to dryness, and the residue was dissolved in ethyl acetate (250 mL). This solution was washed with water and dried over anhydrous magnesium sulfate. The solvent was then removed in vacuo leaving a dark crystalline solid (23.4 g), which was purified by chromatography on silica gel eluting with a gradient of ethyl

acetate/petroleum ether to provide the title compound as a tan crystalline solid (13.75 g), m.p. 91-93 °C.

Step C. 1-(3-Phenacetyl-pyridin-2-yl methyl)carbamic acid benzyl ester

To a stirred solution of 2-(2-formyl-pyrrol-1-ylmethyl)-pyridine-3-carboxylic acid methyl ester of Step B (13.65 g, 55.9 mmol) in methanol (50 mL) was added sodium hydroxide (2.2 g, 55.9 mmol.). The reaction mixture was refluxed under nitrogen for 2 hours, and then the solvent was removed in vacuo. A portion of the residual yellow solid (5 g) was suspended in a mixture of benzyl alcohol (20 mL) and benzene (30 mL). Diphenylphosphoryl azide (6.54 g, 1.2 equiv.) was added, and the reaction was slowly heated to reflux. After refluxing for 1 hour, the mixture was cooled and washed with water, dried over anhydrous magnesium sulfate, filtered and evaporated to dryness to provide the title compound as a tan crystalline solid (4.4 g), m.p. 109-111 °C.

Step D. 9,10-Dihydro-4H-3a, 5, 9-triaza-benzo[f]azulene

A stirred mixture of 1-(3-phenacetyl-pyridin-2-yl methyl)-carbamic acid benzyl ester of Step C (1.0 g), in ethyl acetate (10 mL) containing 10% palladium on charcoal (10 mg.), magnesium sulfate (0.010 g) and 5 drops of acetic acid was hydrogenated at atmospheric pressure until hydrogen uptake ceased. The reaction mixture was then filtered through Celite and the solvent removed in vacuo. The crude product (yellow crystalline solid, 0.530 g) was purified by chromatography on silica gel eluting with a gradient of ethyl acetate in petroleum ether to provide the title product as a yellow crystalline solid, m.p. 171-172 °C.

Step E. (4-Bromo-3-methyl-phenyl)-(4H, 10H- 3a, 5, 9-triaza-benzo[f]azulen-9-yl)-methanone

To a stirred solution of the 9,10-dihydro-4H-3a,5,9-triaza-benzo[f]azulene of Step D (1.0 g) in dichloromethane (10 mL) was added 3-methyl-4-bromobenzoyl chloride (1.39 g) and triethylamine (1.1 mL). After stirring for 2.5 hours, the reaction mixture was washed with water, dried over anhydrous magnesium sulfate, filtered and the solvent removed in vacuo to provide the title product as a tan crystalline solid (2.3 g), which was used without further purification.

Step F. (2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)-(4H,10H-3a, 5, 9-triaza-benzo[f]-azulen-9-yl)-methanone

A stirred mixture of (4-bromo-3-methyl-phenyl)-(4H,10H-3a,5,9-triaza-benzo[f]-azulen-9-yl)-methanone of Step E (1.0 g), 2-trifluoromethyl-boronic acid (1.49 g, 3.0 equiv.), potassium phosphate (2.2 g) and a catalytic amount (0.050 g) of tetrakis(triphenylphosphine) palladium (0) in dioxane (10 mL) was refluxed for 2 hours. The solvent was then removed in vacuo and the residue dissolved in dichloromethane. The solution was then washed with water, dried over anhydrous magnesium sulfate, filtered and evaporated to dryness. The residue was then chromatographed on silica gel eluting with 5% ethyl acetate in dichloromethane to yield a colorless gum which crystallized upon addition of a little diethyl ether to provide the title compound as a cream-colored crystalline solid (0.500 g), m.p. 153-155 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.85 (s, 3H), 5.10 (s, 2H), 5.40 (s, 2H), 5.90 (t, 1H), 6.00 (s, 1H), 6.90 (t, 1H), 6.94 (d, 1H), 7.03 (d, 1H), 7.12 (dd, 1H), 7.23 (d, 1H), 7.28 (s, 1H), 7.37 (d, 1H), 7.58 (t, 1H), 7.68 (t, 1H), 7.80 (d, 1H), 8.27 (d, 1H)

MS [(+)ESI, m/z]: 448 $[M+H]^+$.

Anal. Calcd. for $C_{28}H_{20}F_3N_3O$: C 69.79, H 4.51, N 9.39. Found: C 69.91, H 4.30, N 9.26)

Step G. 2,2,2-Trichloro-1-{[9-(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-9,10-dihydro-4H-3a, 5, 9-triaza-benzo[f]azulen-3-yl}-ethanone

To a solution of (2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)-(4H,10H-3a, 5, 9-triaza-benzo[f]azulen-9-yl)-methanone in methylene chloride was added trichloroacetyl chloride (1.1 equiv.) and triethylamine (1.5 equiv,) After stirring overnight at room temperature, the reaction was washed with water, dried over anhydrous magnesium sulfate, and evaporated to dryness to provide the crude title compound which was used as such in the next step.

Step H. 9-[(2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4yl)carbonyl]-9,10-dihydro-3a, 5, 9-triaza-benzo[f]azulen-3-carboxylic acid

To a solution of 2,2,2-trichloro-1-{[9-(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-9,10-dihydro-4H-3a, 5, 9-triaza-benzo[f]azulen-3-yl}-ethanone of Step G in acetone was added 2.5 N sodium hydroxide (1.0 equiv.). After stirring overnight, the solvent was removed in vacuo leaving the crude sodium salt of the carboxylic acid. This

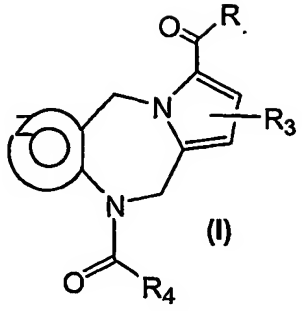
was dissolved in anhydrous ethanol and treated with 2 N hydrochloric acid (1.0 equiv.). The solvent was removed in vacuo, the residue redissolved in anhydrous ethanol and the solvent again removed in vacuo. The crude title compound was then dried in vacuo over phosphorus pentoxide.

Step I. [3-(4-Methyl-piperazine-1-carbonyl)-4H-10H-3a, 5, 9-triaza-benzo[f]azulen-9-yl]-(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)-methanone

To a solution of the 9-[(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4yl)carbonyl]-9,10-dihydro-3a, 5, 9-triaza-benzo[f]azulen-3-carboxylic acid (3.38 mmol) of Step H in N,N-dimethylformamide (20 mL) was added 1-hydroxybenzotriazole (1.1 equiv.) and [3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (1.2 equiv.), followed by 4-methyl-piperazine (1.2 equiv.) and N,N-diisopropylethyl amine (1.5 equiv.). The reaction mixture was stirred overnight, then diluted with ethyl acetate and washed with water and saturated aqueous sodium bicarbonate. The organic phase was dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. Purification of the residue was effected by chromatography on silica gel eluting with a gradient of methanol in ethyl acetate to provide the title compound as a white foam.

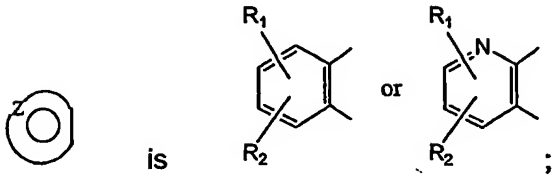
What is Claimed:

1. A compound of the formula:



(I)

wherein:

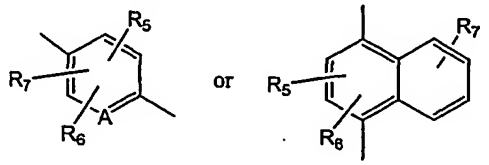


is ; R_1 and R_2 are, independently, selected from hydrogen, (C_1-C_6)alkyl, halogen, cyano, trifluoromethyl, hydroxy, amino, (C_1-C_6alkyl)amino, (C_1-C_6)alkoxy, -OCF_3, (C_1-C_6alkoxy)carbonyl, -NHCO[(C_1-C_6)alkyl], carboxy, -$CONH_2$, –CONH[(C_1-C_6)alkyl], or –CON[(C_1-C_6)alkyl]$_2$;

R_3 is a substituent selected from hydrogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, hydroxy, amino, (C_1-C_6alkyl)amino, -COalkyl(C_1-C_6), or halogen;

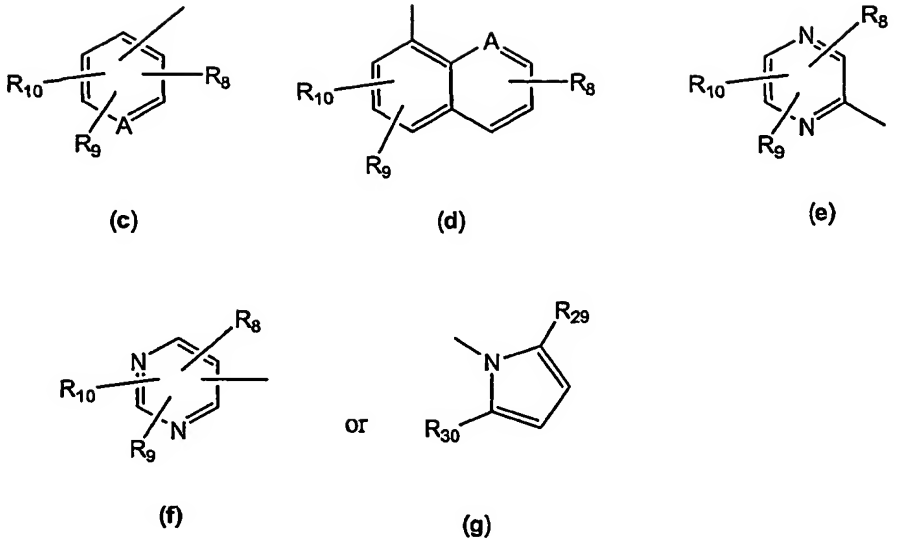
R_4 consists of the moiety **B-C**; wherein:

B is selected from the group of:



(a) (b)

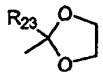
and **C** is selected from the group of:



wherein:

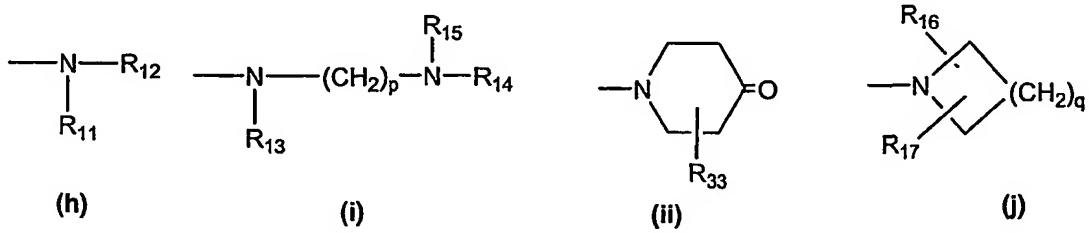
A is CH or N;

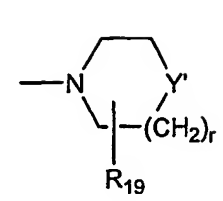
R_5, R_6, R_7, R_8, R_9, R_{10} are, independently, selected from hydrogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6alkyl)carbonyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, acyloxy(C_1-C_6)alkyl, (C_3-C_8)cycloalkyl, formyl, (C_3-C_8cycloalkyl)carbonyl, carboxy, (lower alkoxy)carbonyl, (C_3-C_8cycloalkyl)-oxycarbonyl, aryl(C_1-C_6alkyl)oxycarbonyl, carbamoyl, -O-CH_2-CH=CH_2, halogen, halo lower alkyl, trifluoromethyl, -OCF_3, -S[(C_1-C_6)alkyl], -OC(O)N[(C_1-C_6)alkyl]$_2$, -CONH[(C_1-C_6)alkyl], -CON[(C_1-C_6)alkyl]$_2$, (C_1-C_6)alkylamino, di-[(C_1-C_6)alkyl] amino, di-[(C_1-C_6)alkyl]amino(C_1-C_6)alkyl, hydroxy, cyano, trifluoromethylthio, nitro, amino, (C_1-C_6)alkylsulfonyl, aminosulfonyl, (C_1-C_6)alkylaminosulfonyl,



, phenyl or naphthyl;

and R is selected from -OH, $NHOR_{36}$, or any of the following groups:





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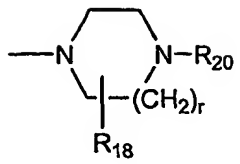
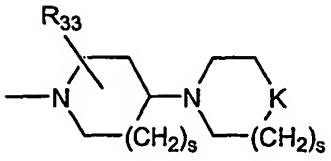
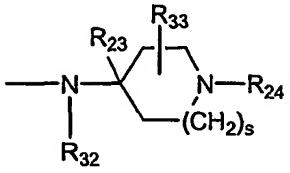


(l)



o



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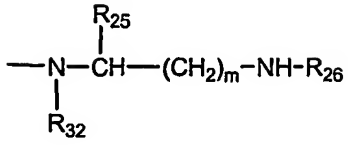
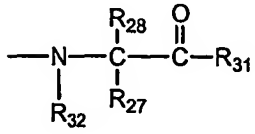


(u)



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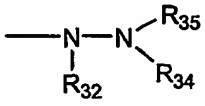

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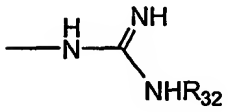

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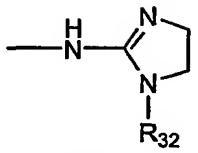

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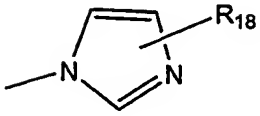

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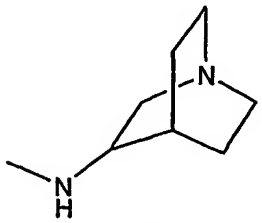
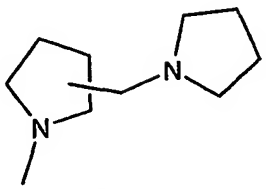
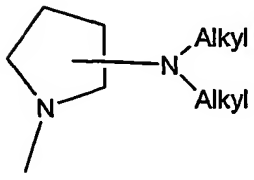


(z')



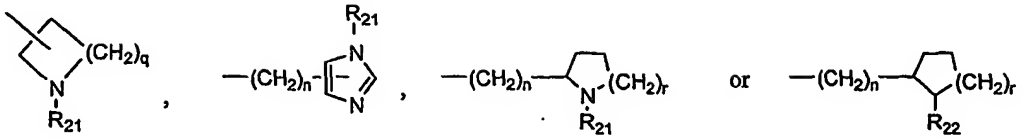
(z'')

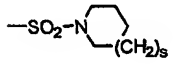
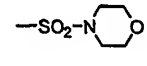


(z''')

5 wherein:

R_{11} and R_{12} are, independently, selected from hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_3\text{-}C_8)$cycloalkyl optionally mono- or di-[$(C_1\text{-}C_6)$alkyl] substituted, polycycloalkyl including but not limited to adamantanyl, adamantane lower alkyl, bornyl, norbornyl, or quinuclidyl;



(C_3-C_8cycloalkyl)loweralkyl, halo lower alkyl, cyano lower alkyl, lower alkyl thiol, loweralkoxycarbonyl lower alkyl, lower alkylthio lower alkyl, indolyl lower alkyl; aryl, optionally substituted with 1 to three substituents selected from the group of lower alkyl, hydroxy, (C_1-C_6)alkoxy, aryl lower alkoxy, halogen, -CF_3, -OCF_3, -$OCHF_2$, -OCH_2F, -OCH_2CF_3, -OCF_2CF_3, -OCH_2CHF_2, loweralkylamido lower alkyl, diloweralkylamido lower alkyl, morpholinyl, thiomorpholinyl, pyrrolidinyl, piperidinyl, -SCF_3, -SO_2[lower alkyl], sulfonyl (C_3-C_8)cycloalkyl,  or  ; or (C_7-C_{12}) arylalkyl, wherein the aryl moiety is optionally substituted with halogen or alkoxy; with the proviso that R_{11} and R_{12} can be taken together with the nitrogen to which they are attached to form an unsaturated heteroaromatic ring containing 2 nitrogen atoms;

R_{13} is selected from hydrogen, (C_1-C_6)alkyl, (C_7-C_{12})aralkyl, or-$(CH_2)_p$-N(lower alkyl)$_2$;

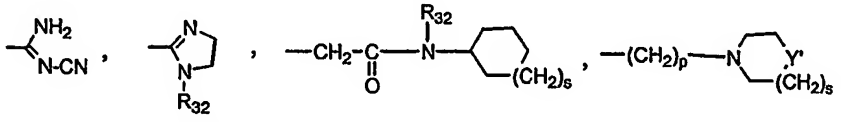
R_{14} and R_{15} are, independently, selected from hydrogen, (C_1-C_6)alkyl, or (C_7-C_{12}) aryl lower alkyl, with the proviso that R_{14} and R_{15} can be taken together with the nitrogen atom to which they are attached to form a 5 to 7 membered saturated heterocycle, optionally containing one additional O or S atom (all of the above rings being optionally substituted with 1 or more (C_1-C_6)alkyl groups); or a 5-membered unsaturated heterocycle containing 1 to 3 nitrogen atoms;

R_{16} and R_{17} are, independently selected from the group of hydrogen, (C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$, (C_7-C_{12}) aryl lower alkyl, lower alkoxy carbonyl, aryl lower alkoxy carbonyl, -$CONH_2$, -CONH [(C_1-C_6)alkyl], -CON [(C_1-C_6) lower alkyl]$_2$; (C_3-C_8)cycloalkylamino (C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$ amino; with the proviso that R_{16} and R_{17} can be joined to form a 5 to 6 membered saturated ring to provide a bicyclic system, optionally containing one or more alkyl groups including, but not limited to, 1,3,3-trimethyl-6-aza-bicyclo[3.2.1]octane;

R_{18} is one to three substituents selected independently from the group of hydrogen, or $(C_1\text{-}C_6)$alkyl;

R_{19} is selcted from the group of hydrogen, $(C_1\text{-}C_6)$alkyl, $-N[(C_1\text{-}C_6)\text{alkyl}]_2$, or $(C_3\text{-}C_8)$cycloalkylamine when Y'= CH_2; or it is selected from the group of hydrogen and $(C_1\text{-}C_6)$alkyl when Y' = X';

R_{20} is selected from the group of hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_3\text{-}C_8)$cycloalkyl, $-CONH_2$, -CON[lower alkyl]$_2$, carbonyl lower alkyl, lower alkyl CONH[lower alkyl], lower alkyl CON[lower alkyl]$_2$, $(C_3\text{-}C_8)$cycloalkylamino carbonyl, $(C_3\text{-}C_8)$cycloalkylaminocarbonyl lower alkyl, arylamino carbonyl lower alkyl, lower alkoxy carbonyl, lower alkoxy carbonyl lower alkyl, $-(CH_2)_p$-N[lower alkyl]$_2$, $-(CH_2)_p$-N[lower alkenyl]$_2$, $-CH[\text{aryl}]_2$ wherein the aryl is optionally substituted by $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, or halogen;



benzodioxolyl, benzodioxolyl lower alkyl, benzodioxanyl, benzodioxanyl lower alkyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, furancarbonyl, $-SO_2$[lower alkyl], aryl optionally substituted by one to three substituents selected independently, from the group of hydrogen, halogen, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, lower alkoxy, $-CF_3$, $-OCF_3$, $-OCH_2CF_3$, $-OCHF_2$, $-OCH_2F$, $-OCF_2CF_3$, $-OCH_2CHF_2$, -CO lower alkyl, -CN, nitro, $-SCH_3$, aryl lower alkoxy, aryl lower alkoxy carbonyl, indolyl, morpholino or thiomorpholino; or $(C_7\text{-}C_{12})$aralkyl wherein the aryl moiety is optionally substituted with halogen, $(C_1\text{-}C_6)$alkyl, or $(C_1\text{-}C_6)$alkoxy;

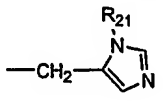
R_{21} and R_{22} are selected, independently, from the group of hydrogen, $(C_1\text{-}C_6)$alkyl, or $(C_7\text{-}C_{12})$ arylalkyl;

R_{23} is selected from hydrogen, or $(C_1\text{-}C_6)$alkyl ;

R_{24} is selected from the group of $(C_1\text{-}C_6)$alkyl, $(C_7\text{-}C_{12})$ arylalkyl, lower alkoxycarbonyl, or $SO_2[(C_1\text{-}C_6)\text{alkyl}]$;

R_{25} is selected from $(C_1\text{-}C_6)$alkyl, $(C_7\text{-}C_{12})$ arylalkyl, lower alkoxycarbonyl, aryllower alkoxycarbonyl, -COOH, $-CONH_2$, $-CONH[(C_1\text{-}C_6)\text{alkyl}]$, $-CONH[(C_7\text{-}C_{12})\text{arylalkyl}]$, $-CON[(C_1\text{-}C_6)\text{alkyl}]_2$, or $-CON[(C_7\text{-}C_{12})\text{ arylalkyl}]_2$;

R_{26} is selected from hydrogen, lower alkoxycarbonyl, fluorenylalkoxycarbonyl, aryl lower alkyl, or aryl lower alkoxycarbonyl;

R_{27} and R_{28} are, independently, selected from the group of hydrogen, lower alkyl, aryl lower alkyl (the aryl moiety being optionally substituted by hydroxy, alkoxy, or halogen), or  ; with the proviso that R_{27} and R_{28} can be taken together with the carbon to which they are attached to form a 3 to 6-membered saturated ring;

R_{29} and R_{30} are, independently, selected from the group of hydrogen, $(C_1$-$C_6)$ lower alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, cyclo lower alkyl, or aryl [optionally substituted by hydroxy, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkyl, halo, cyano, $-SO_2$ [$(C_1$-$C_6)$alkyl, or $-S[(C_1$-$C_6)$alkyl];

R_{31} is selected from the group of hydroxy, $(C_1$-$C_6)$ alkoxy, aryl lower alkoxy, amino, $-NH[(C_1$-$C_6)$alkyl], or $-N[(C_1$-$C_6)$alkyl$]_2$;

R_{32} is selected from the group of hydrogen, or $(C_1$-$C_6)$alkyl;

R_{33} is one to three substituents selected from the group of hydrogen, or $(C_1$-$C_6)$alkyl;

R_{34} and R_{35} are, independently, selected from the group of hydrogen, $(C_1$-$C_6)$alkyl, $(C_7$-$C_{12})$ arylalkyl, with the proviso that R_{34} and R_{35} taken together with the nitrogen atom to which they are attached, may form a 4 to 8 membered saturated heterocycle, optionally containing one additional O, S or $N[(C_1$-$C_6)$alkyl], all the above rings being optionally substituted with 1 or more $(C_1$-$C_6)$alkyl groups; or a 5 membered unsaturated heterocycle containing 2 to 3 nitrogen atoms;

R_{36} is selected from the group of hydrogen, or $(C_1$-$C_6)$alkyl;

X' is O, S, SO, SO_2;

Y'= CH_2 or X';

K= Y' or $N[(C_1$-$C_6)$alkyl];

m is an integer from 1 to 4;

n is an integer from 1 to 4;

p is an integer from 2 to 4 ;

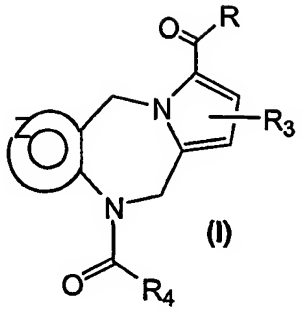
q is an integer from 1 to 5;

r is an integer from 1 to 2;

s is an integer from 0 to 1;

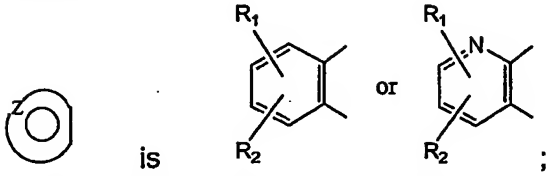
and the pharmaceutically acceptable salts, or pro-drug forms thereof.

2. A compound having the formula:



(I)

wherein:



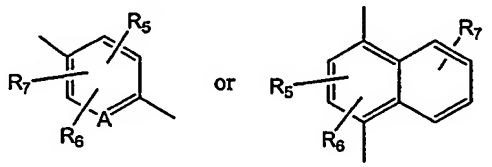
is ;

R_1 and R_2 are, independently, selected from hydrogen, (C_1-C_6)alkyl, halogen, cyano, trifluoromethyl, hydroxy, amino, (C_1-C_6)alkylamino, (C_1-C_6)alkoxy, -OCF_3, (C_1-C_6 lalkoxy)carbonyl, -NHCO[(C_1-C_6)alkyl], carboxy, -$CONH_2$, –CONH[(C_1-C_6)alkyl], or –CON[(C_1-C_6)alkyl]$_2$;

R_3 is a substituent selected from hydrogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, hydroxy, amino, (C_1-C_6)alkylamino, -CO(C_1-C_6)alkyl, or halogen;

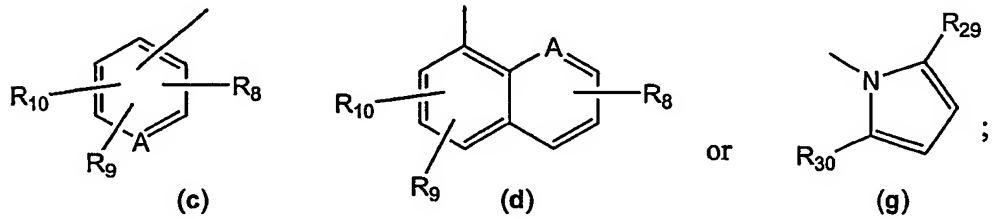
R_4 consists of the moiety **B-C**; wherein:

B is selected from the group of:



(a) (b)

and **C** is selected from the group of:



(c) (d) (g)

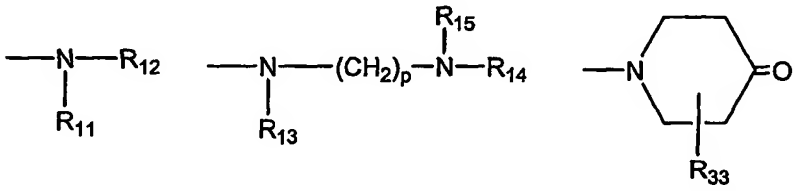
wherein:

A is CH or N;

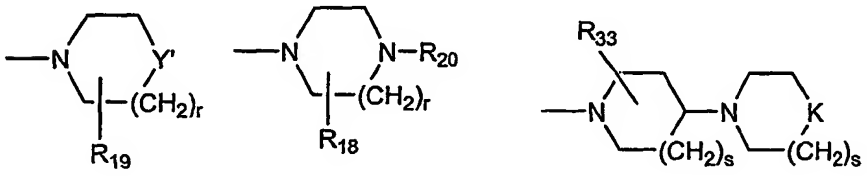
R_5, R_6 , R_7, R_8, R_9, R_{10} are independently selected from hydrogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6alkyl)carbonyl, (C_2-C_6)alkenyl, (C_2-C_6) alkynyl, hydroxy (C_1-C_6) alkyl, loweralkoxy(C_1-C_6)alkyl, C_2-C_7acyloxy(C_1-C_6)alkyl, (C_3-C_8)cycloalkyl, formyl, (C_3-C_8cycloalkyl)carbonyl, carboxy, loweralkoxy carbonyl, (C_3-C_8cycloalkyl)oxycarbonyl, carbamoyl, -O-CH_2-CH=CH_2, halogen, halo lower alkyl including trifluoromethyl, -OCF_3, -S[(C_1-C_6)alkyl], -OC(O)N[(C_1-C_6)alkyl]$_2$, -CONH[(C_1-C_6)alkyl], -CON[(C_1-C_6)alkyl]$_2$, (C_1-C_6)alkylamino, di-[(C_1-C_6)alkyl] amino, (C_1-C_6)alkyl di-[(C_1-C_6)alkyl]amino, hydroxy, cyano, trifluoromethylthio, nitro, amino, (C_1-C_6)alkylsulfonyl, aminosulfonyl, or (C_1-C_6)alkylaminosulfonyl;

R_{29} and R_{30} are, independently, selected from the group of H, C_1-C_6alkyl, (C_2-C_6)lower alkenyl, C_2-C_6alkynyl, or cycloC_3-C_6alkyl;

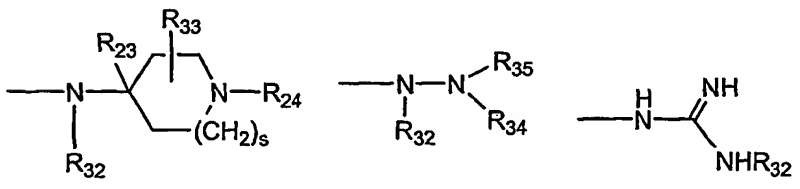
R is selected from lower alkyl, –$NHNH_2$, -$NHOR_{31}$; or -CH=CH-N[R_{32}]$_2$; lower alkoxy; phenyl optionally substituted by from one to three substituents selected from (C_1-C_6)alkyl or halogen ; or a moiety of the formulae:



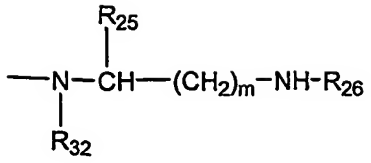
(h) (i) (ii)



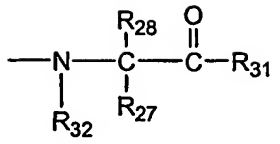
(k) (l) (o)



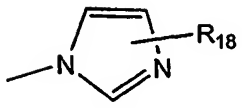
(t) (w) (x)



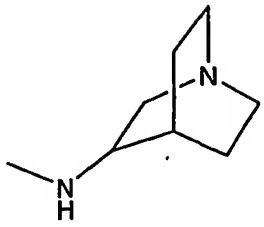
(u)



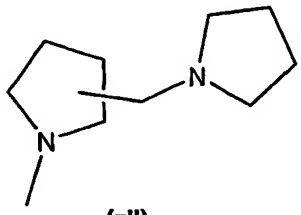
(v)



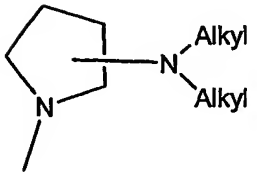
(z)



(z')

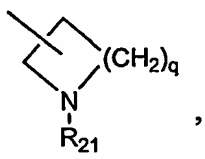


(z")

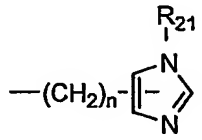


(z"')

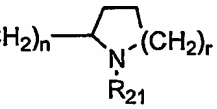
R_{11} and R_{12} are, independently, selected from hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_3\text{-}C_8)$cycloalkyl optionally mono- or di-[$(C_1\text{-}C_6)$alkyl] substituted, $(C_3\text{-}C_8)$-cycloalkyl lower alkyl, halo lower alkyl, cyano lower alkyl, lower alkyl thiol, loweralkoxycarbonyl lower alkyl, or loweralkylthio lower alkyl; or a moiety of the formulae:



,



, or



;

R_{13} is selected from hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_7\text{-}C_{12})$aralkyl, or-$(CH_2)_p$-N(alkyl)$_2$;

R_{14} and R_{15} are, independently, selected from hydrogen, $(C_1\text{-}C_6)$alkyl, with the proviso that R_{14} and R_{15} can be taken together with the nitrogen atom to which they are attached to form:

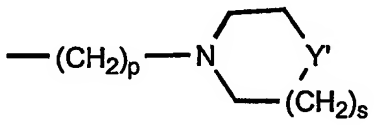
a) a 5 to 7 membered saturated heterocycle, optionally substituted with 1 or more alkyl groups; or

b) a 5-membered unsaturated heterocycle containing 1 to 3 nitrogen atoms;

R_{18} is one to three substituents selected independently from the group of hydrogen, or $(C_1\text{-}C_6)$alkyl;

R_{19} is selcted from the group of hydrogen, $(C_1\text{-}C_6)$alkyl, $-N[(C_1\text{-}C_6)\text{alkyl}]_2$, or $(C_3\text{-}C_8)$cycloakylamine when Y'= CH_2; or it is selected from the group of hydrogen and $(C_1\text{-}C_6)$ lower alkyl when Y' = X';

R_{20} is selected from the group of hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_3\text{-}C_8)$cycloalkyl, $-CONH_2$, -CON[lower alkyl]$_2$, carbonyl lower alkyl, lower alkyl CONH[lower alkyl], lower alkyl CON[lower alkyl]$_2$, lower alkoxy carbonyl, $(CH_2)_p$-N[lower alkyl]$_2$, $-(CH_2)_p$-N[lower alkenyl]$_2$, -CH[phenyl]$_2$ wherein the phenyl ring is optionally substituted by $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, or halogen; or R_{20} is a moiety of the formula:



;

R_{21} and R_{22} are selected, independently, from the group of hydrogen, $(C_1\text{-}C_6)$alkyl, or $(C_7\text{-}C_{12})$ arylalkyl;

R_{23} is selected from hydrogen, cyano or $(C_1\text{-}C_6)$alkyl ;

R_{24} is selected from the group of $(C_1\text{-}C_6)$alkyl, lower alkoxycarbonyl, or $SO_2[(C_1\text{-}C_6)\text{alkyl}]$;

R_{25} is selected from $(C_1\text{-}C_6)$alkyl, lower alkoxycarbonyl, -COOH, $-CONH_2$, $-CONH[(C_1\text{-}C_6)\text{alkyl})]$, or $-CON[(C_1\text{-}c_8)\text{alkyl})]_2$;

R_{26} is selected from hydrogen, lower alkoxycarbonyl, or fluorenylalkoxycarbonyl;

R_{27} and R_{28} are, independently, selected from the group of hydrogen or lower alkyl; with the proviso that R_{27} and R_{28} can be taken together with the carbon to which they are attached to form a 3 to 6-membered saturated ring;

R_{31} is selected from the group of hydroxy, $(C_1\text{-}C_6)$alkoxy, amino, $-NH[(C_1\text{-}C_6)\text{alkyl}]$, or $-N[(C_1\text{-}C_6)\text{alkyl}]_2$;

R_{32} is elected from the group of hydrogen, or $(C_1\text{-}C_6)$alkyl;

R_{33} is one to three substituents selected from the group of hydrogen, or $(C_1\text{-}C_6)$alkyl;

R_{34} and R_{35} are, independently, selected from the group of hydrogen, or $(C_1\text{-}C_6)$alkyl, with the proviso that R_{34} and R_{35} taken together with the nitrogen atom to which they are attached, may form a 5 membered unsaturated heterocycle containing 2 to 3 nitrogen atoms;

X' is O;

Y'= CH_2 or X';

K= Y' or N[(C_1-C_6)alkyl];

m is an integer from 1 to 4;

n is an integer from 1 to 4;

p is an integer from 2 to 4 ;

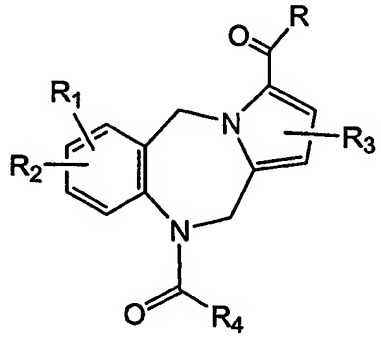
q is an integer from 1 to 5 ;

r is an integer from 1 to 2;

s is an integer from 0 to 1;

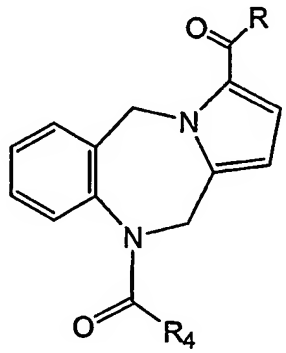
and the pharmaceutically acceptable salts, or pro-drug forms thereof.

3. A compound of Claim 2 having the formula:



wherein R and R_4 are as defined in Claim 2, or a pharmaceutically acceptable salt thereof.

4. A compound of Claim 2 having the formula:



wherein R and R_4 are as defined in Claim 2, or a pharmaceutically acceptable salt thereof.

5. A compound of Claim 1 which is selected from the group of:

a) 10-[(2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid;

b) (4-Methyl-piperazin-1-yl)-[10-(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-3-yl-methanone;

c) 10-[(2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid bis-(3-dimethylamino-propyl)-amide;

d) [4-(3-Dimethylaminopropyl)-piperazin-1-yl]-[10-(2-methyl-2'-trifluoro-methyl-[1,1'-biphenyl]-4-yl)carbonyl]-[10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl]-methanone;

e) [3-Methyl-4-(3-methyl-phenyl)-piperazin-1-yl]-[10-(2-methyl-2'-trifluoro-methyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl-methanone;

f) 4-[[10,11-Dihydro-10-[[2-methyl-2'-trifluoromethyl[1,1'-biphenyl]-4-yl]-carbonyl]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl]carbonyl]-1-piperazine-carboxylic acid, tert-butyl ester;

g) 10,11-Dihydro-10-[[2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]-carbonyl]-3-(1-piperazinylcarbonyl)-5H-pyrrolo[2,1-c][1,4]benzodiazepine;

h) N-[(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)carbonyl]guanidine;

i) 10-[(2'-Methoxy-2-methyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo [2,1-c][1,4]benzodiazepine-3-carboxylic acid; or

j) 10-[(3-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxylic acid;

or a pharmaceutically acceptable salt form thereof.

6. A compound of Claim 1 which is selected from the group of:

N-Methyl-N-[3-(dimethylamino)propyl]-10-[(3-methoxy-2'-methyl[1,1'-biphenyl]- 4-yl)carbonyl]- 10,11-dihydro-5H-pyrrolo[2,1- c][1,4]benzodiazepine-3-carboxamide;

7,8-Dimethoxy-[10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl][2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]methanone;

N-Methyl-[N-(3-dimethylamino)propyl]-7,8-dimethoxy-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxamide;

7,8-Dimethoxy-10-{[2-methyl-2'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl]carbonyl}-[(10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)carbonyl]-4-piperidinone;

10-{[6-Chloro-3-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid;

10-{[2'-Chloro-6-chloro-3-methoxy-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid;

10-{[6-Chloro-3-methoxy-2'-ethoxy[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine;

10-{[6-Chloro-3-methoxy-2'-fluoro-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid;

10-{[2-Methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid;

{[10-(2-Methoxy)-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-[(2S)-[(2-pyrrolidin-1-yl)methyl]pyrrolidin-1-yl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl-methanone;

N-Methyl-[N-(3-dimethylamino)propyl]-10-{[2-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-3-carboxamide;

N-Methyl-[N-(2-dimethylamino)ethyl]-10-{[2-methoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

[2-Chloro-4-(naphthalen-1-yl)phenyl][10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-10-yl]methanone;

[4-(4-Methyl-naphthalen-1-yl)phenyl][10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-10-yl]methanone;

Methyl 10-{[2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1.4] benzodiazepine-8-carboxylate;

[4-(2,5-Dimethyl-1-H-pyrrol-1-yl)-3-methoxy-phenyl] [10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl] methanone;

[6-(Naphthalen-1-yl)-pyridin-3-yl]-[10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-10-yl]methanone;

(6-Phenyl-pyridin-3-yl)-[10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepin-10-yl]methanone;

[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3,5-dimethyl-phenyl][10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-10-yl]methanone;

[3-Methyl-4-(4-pyridinyl)phenyl]-[10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-10-yl]methanone;

10-{[3,6-Dimethoxy-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine;

{[10-(2-Methoxy)-2'-chloro-[1,1'-biphenyl]-4-yl]carbonyl}-[(2S)-[(2-pyrrolidin-1-yl)-methyl]pyrrolidin-1-yl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl-methanone;

10-[(6-Chloro-3-methoxy-2'-ethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methylpiperidin-4-yl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-N-methyl-10-[(6-chloro-3-methoxy-2'-fluoro[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

[4-(3-Dimethylaminopropyl)-piperazin-1-yl]-{10-[4-(naphthalen-1-yl)-phenyl]-carbonyl}-10,11-dihydro-5H-pyrrolo [2,1-c] [1,4]benzodiazepin-3-yl-methanone;

(4-Methyl-piperazin-1-yl)-{10-[2-chloro-[4-(naphthalen-1-yl)]phenyl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl-methanone;

10-{[2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-8-(piperidine-1-carbonyl)-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxylic acid-methyl-(1-methyl-piperidin-4-yl)-amide;

[3-Methyl-4-(pyridin-4-yl)-phenyl]-{[(2S)-3-[(2-pyrrolidin-1-yl)methyl]pyrrolidin-1-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-10-yl-methanone;

10-[(6-Phenyl-pyridin-3-yl)carbonyl]- N-methyl-N-(1-methyl-piperidin-4-yl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;
or a pharmaceutically acceptable salt form thereof.

7. A compound of Claim 1 which is selected from the group of:

[4-(3-Dimethylaminopropyl)-piperazin-1-yl]-[10-[(2'-methoxy-2-methyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl]-methanone;

N-[2-(Dimethylamino)ethyl]-10-{[6-chloro-3-methoxy-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4] benzodiazepin-3 carboxamide;

10-[(2'-Chloro-6-chloro-3-methoxy-[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methylpiperidin-4-yl)-10,11-dihydro-5H-pyrrolo [2,1-c][1,4] benzodiazepine-3-carboxamide;

{3-[4-(3-Dimethylamino-propyl)-piperazin-1-yl]carbonyl}-[4-(4-methyl-naphthalen-1-yl)phenyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-10-yl-methanone;

10-{[6-(Naphthalen-1-yl)-pyridin-3-yl]carbonyl}- N-methyl-N-(1-methyl-piperidin-4-yl)-10,11-dihydro-5H-pyrrolo[1,2-c][1,4]benzodiazepine-3-carboxamide;

{[10-(3,6-Dimethoxy)-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl]carbonyl}-[(2S)-[(2-pyrrolidin-1-yl)methyl]-pyrrolidin-1-yl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzo-diazepine-3-yl-methanone;

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

{10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

{10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

{10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

{10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

{10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

{10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

{10-[3-Methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

(4-Methyl-1,4-diazepan-1-yl)(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)methanone;

8. A compound of Claim 1 which is selceted from the group of:

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

{10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

{10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

{10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

{10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

{10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

{10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

{10-[3-Methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

N-[3-(Dimethylamino)propyl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-10-[(2,2'-dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethyl-amino)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)-propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;
or a pharmaceutically acceptable salt form thereof.

9. A compound of Claim 1 which is selected from the group of:

N-[3-(Dimethylamino)propyl]-10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[2-Chloro-4-(1-naphthyl)benzoyl]-N-[3-(dimethylamino)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]-carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1.4]benzodiazepine-3-carboxamide;

N-[2-(Dimethylamino)ethyl]-N-methyl-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(dimethylamino)ethyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(dimethylamino)ethyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[2-(Dimethylamino)ethyl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[2-(Dimethylamino)ethyl]-10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[2-(Dimethylamino)ethyl]-10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[2-(Dimethylamino)ethyl]-N-methyl-10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[2-(Dimethylamino)ethyl]-10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[2-(Dimethylamino)ethyl]-10-[3-methoxy-4-(1-naphthyl)benzoyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(dimethylamino)ethyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(dimethylamino)ethyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[2-Chloro-4-(1-naphthyl)benzoyl]-N-[2-(dimethylamino)ethyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-N-methyl-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)propyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)-propyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide; or a pharmaceutically acceptable salt form thereof.

10. A compound of Claim 1 which is selcetd from the group of:

N-[3-(Dimethylamino)propyl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-10-[(2,2'-dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-N-methyl-10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-10-[3-methoxy-4-(1-naphthyl)benzoyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)propyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(dimethylamino)propyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[2-Chloro-4-(1-naphthyl)benzoyl]-N-[3-(dimethylamino)propyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl] methanone;

{10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone;

{10-[(2-Methyl-2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone;

{10-[(2-Methyl-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone;

{10-[(2-Methyl-3'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone;

{10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone;

{10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone;

{10-[(6-Chloro-3-methoxy-3'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl] methanone;

{10-[3-Methoxy-4-(1-naphthyl)-benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone;

{10-[(2,2'-Dimethoxy-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone;
or a pharmaceutically acceptable salt form thereof.

11. A compound of Claim 1 which is selcetewd from the group of:

{10-[(2,3'-Dimethoxy-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone;

{10-[(2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]methanone;

{10-[(2-Methyl-2'-(trifluoromethyl) -[1,1'-biphenyl]-4-yl)carbonyl]- 10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl] methanone;

N-[3-(1H-Imidazol-1-yl)propyl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(1H-imidazol-1-yl)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(1H-Imidazol-1-yl)propyl]-10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(1H-Imidazol-1-yl)propyl]-10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(1H-Imidazol-1-yl)propyl]-10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(1H-Imidazol-1-yl)propyl]-10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(1H-imidazol-1-yl)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(1H-imidazol-1-yl)-propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(1H-Imidazol-1-yl)propyl]-10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(1H-imidazol-1-yl)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[3-(1H-imidazol-1-yl)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[2-Chloro-4-(1-naphthyl)benzoyl]-N-[3-(1H-imidazol-1-yl)propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(1H-Imidazol-1-yl)propyl]-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

{10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

{10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

{10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

{10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;
or a pharmaceutically acceptable salt form thereof.

12. A compound of Claim 1 which is selected from the group of:

{10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

{10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

{10-[3-Methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

(10-{[2-Methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)-ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[3-Methoxy-4-(1-naphthyl)benzoyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;
or a pharmaceutically acceptable salt form thereof.

13. A compound of Claim 1 which is selected from the group of:

10-[2-Chloro-4-(1-naphthyl)benzoyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-{[2-Methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-N-[2-(1-piperidinyl)-ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)-ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[3-Methoxy-4-(1-naphthyl)benzoyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)-ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-[2-(1-methyl-2-pyrrolidinyl)-ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[2-Chloro-4-(1-naphthyl)benzoyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[2-(1-Methyl-2-pyrrolidinyl)ethyl]-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-Methyl-10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide; or a pharmaceutically acceptable salt form thereof.

14. A compound of Claim 1 which is selected from the group of:

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[3-Methoxy-4-(1-naphthyl)benzoyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-4-piperidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-Methyl-N-(1-methyl-4-piperidinyl)-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-Methyl-10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[3-Methoxy-4-(1-naphthyl)benzoyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-N-methyl-N-(1-methyl-3-pyrrolidinyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-Methyl-N-(1-methyl-3-pyrrolidinyl)-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}-methanone;

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)-methanone;

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(dimethylamino)ethyl]-1-piperazinyl}-methanone;

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[(2,2'-dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}-methanone;
or a pharmaceutically acceptable salt form thereof.

15. A compound of Claim 1 which is selected from the group of:

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[(2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}-methanone;

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(dimethylamino)ethyl]-1-piperazinyl}-methanone;

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}{4-[2-(dimethylamino)ethyl]-1-piperazinyl}methanone;

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}{4-[2-(dimethylamino)ethyl]-1-piperazinyl}methanone;

{10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone;

{10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone;

{10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone;

{10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone;

{10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone;

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone;

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}-methanone;

{10-[3-Methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone;

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone;

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone;

(10-{[2-Methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl){4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}-methanone;

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}-methanone;

{10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone;

(4-Allyl-1-piperazinyl){10-[(6-chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;
or a pharmaceutically acceptable salt form thereof.

16. A compound of Claim 1 which is selected from the group of:

(4-Allyl-1-piperazinyl){10-[(2,2'-dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Allyl-1-piperazinyl){10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Allyl-1-piperazinyl){10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Allyl-1-piperazinyl){10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Allyl-1-piperazinyl){10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Allyl-1-piperazinyl){10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Allyl-1-piperazinyl){10-[(6-chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Allyl-1-piperazinyl){10-[(2,2'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Allyl-1-piperazinyl){10-[(2,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Allyl-1-piperazinyl){10-[2-chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Allyl-1-piperazinyl)(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]-carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)methanone;

(4-Allyl-1-piperazinyl){10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Isopropyl-1-piperazinyl){10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone;

(4-Isopropyl-1-piperazinyl){10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Isopropyl-1-piperazinyl){10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Isopropyl-1-piperazinyl){10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

(4-Isopropyl-1-piperazinyl){10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone;

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone;
or a pharmaceutically acceptable salt form thereof.

17. A compound of Claim 1 which is selected from the group of:

(4-Isopropyl-1-piperazinyl)(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]-carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)methanone;

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone;

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone;

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone;

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone;

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}-methanone;

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[(2'-methoxy[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[(2,2'-dimethyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}-methanone;

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[(2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}-methanone;

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[3-(dimethylamino)propyl]-1-piperazinyl}-methanone;

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[3-(dimethylamino)propyl]-1-piperazinyl}-methanone;

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[3-methoxy-4-(1-naphthyl)-benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}{4-[3-(dimethylamino)propyl]-1-piperazinyl}methanone;

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}{4-[3-(dimethylamino)propyl]-1-piperazinyl}methanone;

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}{4-[3-(dimethylamino)propyl]-1-piperazinyl}methanone;

{10-[(2-Methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}{4-[3-(dimethylamino)propyl]-1-piperazinyl}-methanone;

(10-{[2-Methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]-methanone;

{10-[(2'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1pyrrolidinylmethyl)pyrrolidinyl] methanone; or a pharmaceutically acceptable salt form thereof.

18. A compound of Claim 1 which is selected from the group of:

{10-[(2,2'-Dimethyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone;

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone;

{10-[3-Methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone;

{10-[(3'-Methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone;

{10-[(2'-Methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone;

{10-[(2'-Methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone;

{10-[(2-Methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone;

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]-methanone;

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]-methanone;

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone;

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl)pyrrolidinyl]methanone;

[(3R)-3-(Dimethylamino)pyrrolidinyl](10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)-methanone;

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{10-[(6-Chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[(3R)-3-(dimethylamino)pyrrolidinyl]methanone;

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[(2,2'-dimethyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{10-[(6-Chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[(3R)-3-(dimethylamino)pyrrolidinyl]methanone;

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{10-[2-Chloro-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepin-3-yl}[(3R)-3-(dimethylamino)pyrrolidinyl]methanone;

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[(2'-methoxy[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;
or a pharmaceutically acceptable salt form thereof.

19. A compound of Claim 1 which is selected from the group of:

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[(2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[(3R)-3-(dimethylamino)pyrrolidinyl]methanone;

{10-[(2,3'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}[(3R)-3-(dimethylamino)pyrrolidinyl]methanone;

N-[(1S)-2-Amino-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[(1S)-2-Amino-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[(1S)-2-Amino-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-10-[(2,2'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[(1S)-2-Amino-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-10-[(6-chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]-benzodiazepine-3-carboxamide;

N-[(1S)-2-Amino-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

1H-Imidazol-1-yl{10-[(3'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

1H-Imidazol-1-yl{10-[(2-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

1H-Imidazol-1-yl{10-[3-methoxy-4-(1-naphthyl)benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

1H-Imidazol-1-yl{10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{10-[(2,2'-Dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c]-[1,4]benzodiazepin-3-yl}(1H-imidazol-1-yl)methanone;

1H-Imidazol-1-yl(10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl)methanone;

N-[(3S)-1-Azabicyclo[2.2.2]oct-3-yl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[(3R)-1-Azabicyclo[2.2.2]oct-3-yl]-10-[(2'-methoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[(3S)-1-Azabicyclo[2.2.2]oct-3-yl]-10-[(6-chloro-3-methoxy-2'-methyl-[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[(3R)-1-Azabicyclo[2.2.2]oct-3-yl]-10-[(2'-methoxy-2-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[(3R)-1-Azabicyclo[2.2.2]oct-3-yl]-10-[(2,2'-dimethoxy[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;
or a pharmaceutically acceptable salt form thereof.

20. A compound of Claim 1 which is selected from the group of:

N-[(3S)-1-Azabicyclo[2.2.2]oct-3-yl]-10-[(2,2'-dimethoxy[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[(3R)-1-Azabicyclo[2.2.2]oct-3-yl]-10-{[2-methyl-2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]carbonyl}-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

tert-Butyl (5S)-6-amino-5-[({10-[(6-chloro-3,3'-dimethoxy[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}carbonyl)amino]-6-oxohexylcarbamate;

tert-Butyl (5S)-6-amino-5-[({10-[(2,2'-dimethoxy[1,1'-biphenyl]-4-yl)carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}carbonyl)amino]-6-oxohexylcarbamate;

tert-Butyl (5S)-6-amino-5-[({10-[(6-chloro-3-methoxy-2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}carbonyl)amino]-6-oxohexylcarbamate;

{10-(3-Methoxy-4-pyridin-3-yl-benzoyl)-10,11-dihydro-5H-pyrrolo[1,2-c][1,4]-benzodiazepin-3-yl}-[4-(1-piperidinyl)-1-piperidinyl]-methanone;

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1-piperazinyl)methanone;

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-methyl-1,4-diazepan-1-yl)methanone;

N-[3-(Dimethylamino)propyl]-10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxy-benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[2-(Dimethylamino)ethyl]-10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxy-benzoyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

N-[3-(Dimethylamino)propyl]-10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxy-benzoyl]-N-methyl-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxy-benzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-piperidinyl)-1-piperidinyl]-methanone;

10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-N-[3-(1H-imidazol-1-yl)-propyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[4-(1-pyrrolidinyl)-1-piperidinyl]methanone;

10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-N-[2-(1-piperidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide;

{4-[2-(Dimethylamino)ethyl]-1-piperazinyl}{10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}{4-[2-(4-morpholinyl)ethyl]-1-piperazinyl}methanone;

(4-Allyl-1-piperazinyl){10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}(4-isopropyl-1-piperazinyl)methanone;

{4-[3-(Dimethylamino)propyl]-1-piperazinyl}{10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

{10-[4-(2,5-Dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo-[2,1-c][1,4]benzodiazepin-3-yl}[(2S)-2-(1-pyrrolidinylmethyl) pyrrolidinyl]methanone;

[(3R)-3-(Dimethylamino)pyrrolidinyl]{10-[4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-methoxybenzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl}methanone;

[3-(4-Methyl-piperazine-1-carbonyl)-4H-10H-3a, 5, 9-triaza-benzo[f]azulen-9-yl]-(2-methyl-2'-trifluoromethyl-[1,1'-biphenyl]-4-yl)-methanone;
or a pharmaceutically acceptable salt form thereof.

21. A method of treating disorders which are remedied or alleviated by oxytocin antagonist activity in a mammal, the method comprising administering to the mammal in need thereof a pharmaceutically effective amount of a compound as claimed in anyone of claims 1 to 20, or a pharmaceutically acceptable prodrug form thereof.

22. A method of Claim 21 wherein the the disorder which is remedied or alleviated by oxytocin antagonist activity is selected from the group of preterm labor, dysmenorrhea or endometritis.

23. A method for suppressing labor prior to caesarean delivery in a mammal, the method comprising administering to the mammal in need thereof a pharmaceutically effective amount of a compound as claimed in anyone of claims 1 to 20, or a pharmaceutically acceptable salt form thereof.

24. A pharmaceutical composition comprising a compound as claimed in anyone of claims 1 to 20, or a pharmaceutically acceptable prodrug form thereof, or a pharmaceutically acceptable salt form thereof., and a pharmaceutically acceptable carrier or excipient.

INTERNATIONAL SEARCH REPORT

Intern I Application No
PCT/US 02/11527

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D487/04 C07D487/14 A61K31/5517 A61P25/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 521 173 A (VENKATESAN ARANAPAKAM M ET AL) 28 May 1996 (1996-05-28) cited in the application . column 2, line 21 - line 30; claim 1; examples 2,3,5,7-9	1-24
Y	US 5 516 774 A (ALBRIGHT, JAY D. ET AL) 14 May 1996 (1996-05-14) column 2, line 19 - line 26; claim 1; examples 580,592-594	1-24

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 July 2002	01/08/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Seelmann, I

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